The Synthesis of Polar Substituted Norbornenes and the Study of their ^{13}C Chemical Shift and Stereoelectronic Properties

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A Thesis

Submitted in partial fulfilment

of the requirements for the Degree

of

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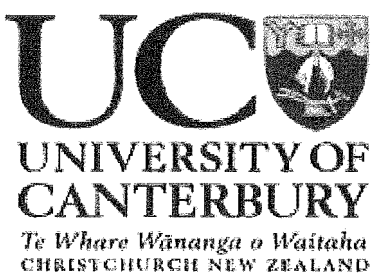
by

Thomas Francis



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ABSTRACT

This thesis represents an attempt to investigate the mode of operation of electronic effects on the C=C bond in 5-substituted-2-norbornenes. A total of 14 *exo* and 9 *endo* derivatives were prepared for study. In the first instance their ^{13}C NMR spectra were obtained, and the effects of these substituents on the chemical shifts of the two alkene carbon atoms were investigated. The role of the polar and resonance effects of the substituent in influencing these by polarising the π electrons of the double bond was explored. It was found that the polar effect of the substituent distorted the π system; but that although –I substituents led to a build up of electron density on the nearer of the two carbons as expected, this build up was less than expected and suggested that part of the charge was being delocalised into the saturated norbornyl framework in some way. Attempts to correlate substituent effects with Hammett substituent constants of various types were unsuccessful.

Next the regiochemistry of the addition of phenylselenenyl chloride to the same alkenes was studied. The ratio of the addition products formed was found to be controlled by the electronic nature of these substituents, although in the case of the *endo* substituted compounds steric effects appeared to play an important role in some cases.

Lastly, the ability of the double bond in 2-norbornene to interact with a C5-X bond was investigated by measuring the effect on the length of the C-X bond by X-ray diffraction. A series of derivatives where X was a good leaving group (nucleofuge) was prepared and their structures were determined. It was hoped to show that the C-X bonds were longer when X was *exo* than when it was *endo*, indicating that the bond in the first had been weakened by the π bond of the alkene interacting with the back orbital of the C-X bond. Unfortunately the crystals showed considerable disorder, and this affected the reliability of the bond lengths obtained to such an extent that the results obtained proved inconclusive.

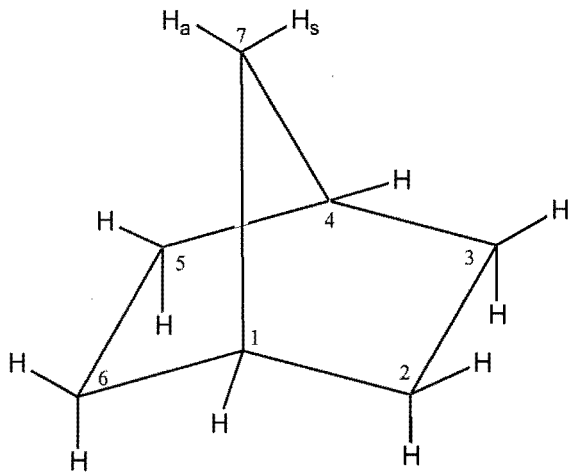
Abbreviations

br s	broad singlet (in NMR)
CIGAR	**C**onstant time **I**nverse-**D**etection **G**radient **A**ccordion **R**escaled (heteronuclear multiple bond correlation spectroscopy)
COSY	**C**orrelation **S**pectroscopy
d	doublet (in NMR)
DCM	dichloromethane
DMAP	dimethylaminopyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
GHSQC	**G**radient **H**eteronuclear **S**ingle-**Q**uantum **C**oherence (NMR)
HPLC	**H**igh **P**erformance **L**iquid **C**hromatography
NMR	**N**uclear **M**agnetic **R**esonance
NOESY	**N**uclear **O**verhauser **E**nhancement **S**pectroscopy (NMR)
m	multiplet (NMR)
PPA	polyphosphoric acid
PPE	Poly Phosphate Ester
s	singlet (NMR)
t	triplet (NMR)
THF	tetrahydrofuran
TLC	**T**hin **L**ayer **C**hromatography

Chapter 1

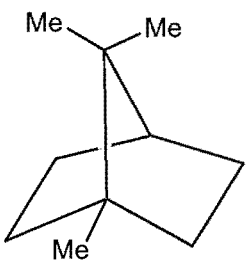
INTRODUCTION

There are a relatively small number of bicyclic systems known in which the rings share more than two carbons, and of these, the most commonly encountered and widely studied is the one based on [2.2.1]bicycloheptane, commonly known as the norbornane.

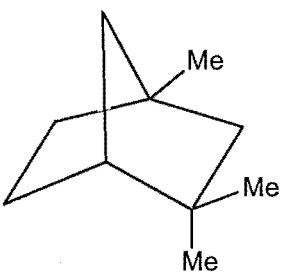


[2.2.1]bicycloheptane

Derivatives of the trimethyl[2.2.1]bicycloheptanes *camphane* and *fenchane* are widely distributed in nature and are members of the class of natural products known as the monoterpenes.

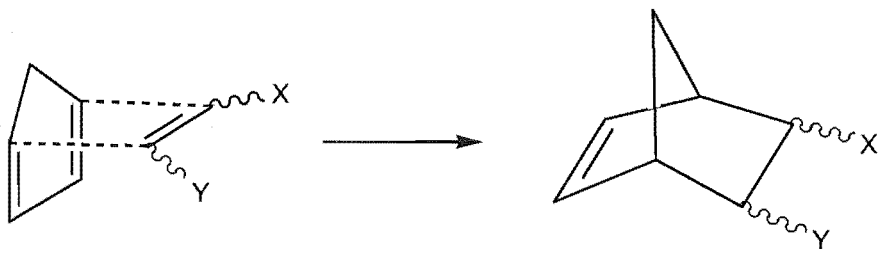


camphane



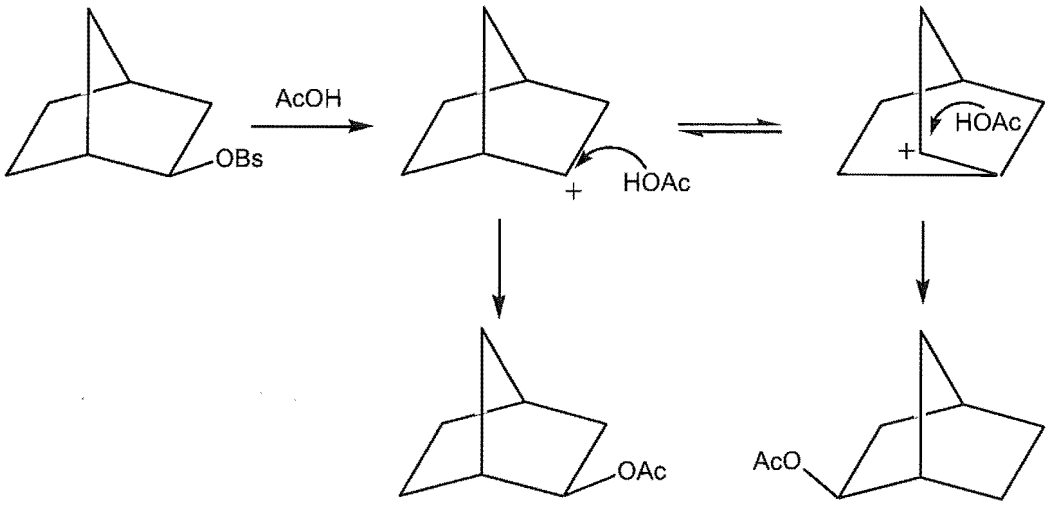
fenchane

While neither [2.2.1]bicycloheptane nor derivatives of it occur in nature, many are readily accessible via the Diels-Alder reaction of cyclopentadiene with a suitable dieneophile:

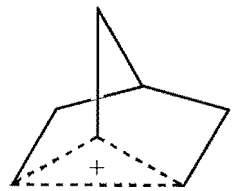


The chemistry of the [2.2.1]bicycloheptyl system has been quite intensively studied. The driving force for many of the investigations was the early observations by terpene chemists that many reactions of derivatives of the bicyclic monoterpenes appeared to undergo skeletal rearrangements when they were reacted, and that such rearrangements appeared to involve carbocationic intermediates. (The occurrence of such rearrangements enormously complicated early attempts to establish terpene structures.). These rearrangements were known as Wagner-Meerwein rearrangements. Once it was recognised that they involved isomerisation of carbocations that resulted from of 1,2 anionotropic migrations of carbons or hydrogens, the structural changes that accompanied the terpene rearrangements could not only be understood, but could even be predicted.

In 1949 Winstein and Trifan[1] reported that optically active 2-*exo*-norbornyl *p*-bromobenzenesulfonate underwent solvolysis in glacial acetic acid to give racemic 2-*exo*-norbornyl acetate. Formation of the racemic product could be rationalised by assuming 50% of the product was derived from attack by the acetic acid on C2, and 50% from attack on a rearranged cation in which the charge was on the carbon that was formerly C1.



Formation of the racemate required that the two cations equilibrated sufficiently rapidly that the attacking acetic acid could not distinguish between them. However Winstein believed that this interpretation was incorrect. He believed that instead of the intermediate cation consisting of an equilibrating mixture of the two "classical" ones, a single "nonclassical" cation with the positive charge shared by C1, C2, and C6 was the actual species present.



This suggestion, which proposed the delocalisation of sigma bonds, although not without precedent (it was accepted that it existed in the boron hydrides) was not universally accepted. H.C. Brown, in particular, strongly favoured a "fast equilibrium between classical ions" interpretation. During the next 30 or so years a considerable amount of time and effort was expended by many researchers in trying to distinguish between the two proposals. What rapidly became very clear was that there was not a lot of difference between the energies of the "non-classical" and the "classical" cations. There is now general agreement that Winstein's interpretation is correct, at least with respect to the 2-norbornyl cation. The situation in substituted 2-norbornenes is less clear cut. The presence of an electron donating substituent on C2 can affect the classical/non-classical balance sufficiently for the classical species to be of lower energy. For

example, it has been shown that for the 1,2-dimethyl-2-norbornyl cation the classical structure is more stable than the non-classical one, and so with this system one is dealing with a pair of equilibrating classical cations[2,3].

Most of the investigations involved reactions of the 2-norbornyl cation itself, usually generated by S_N1 loss of a good leaving group during solvolysis. There have been far fewer investigations of the effect of substituents on these reactions, even though the effect of introducing a substituent is a very well established probe for investigating such systems. Those derivatives likely to be of greatest interest were ones bearing a substituent on C6 since it would be expected to have a substantial effect on the properties of a non-classical cation, but a much lesser one on a classical one. The main investigator working in this area was Grob, who published a number of papers on the solvolysis of both *exo* and *endo* 6-X-2-norbornyl *exo* and *endo* tosylates[4]. He concluded that

(a) The relative solvolysis rates were mainly influenced by the polar effect of X

(b) When the tosylate leaving group was *endo* the rate of solvolysis was only about half as sensitive to the polar effect of X as when it was *exo*.

(d) When the tosylate group was *exo* the sensitivity to the polar effect of X was greater when X was *exo* than when it was *endo*.

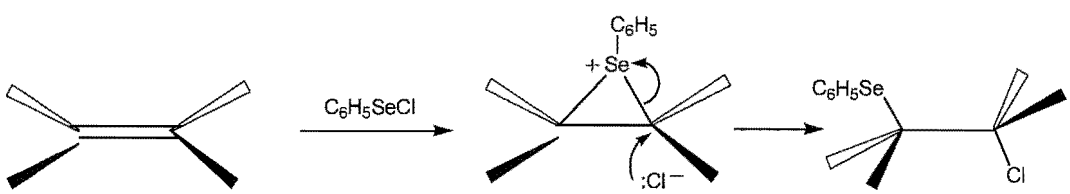
Grob believed that the enhanced sensitivity observed when the tosylate leaving group was *exo* arose as a result of interaction between the back lobe of the C—X sigma orbital and the developing positive charge on C2. This led to an enhanced transmission of the polar effect from the substituent to the reaction site.

The solvolysis reactions studied by Grob took place rather slowly. They gave mixtures of products, the structures of which suggested that skeletal rearrangement was occurring, and that (presumably non-classical) carbocations were intermediates in the reaction. The types of interactions he proposed would

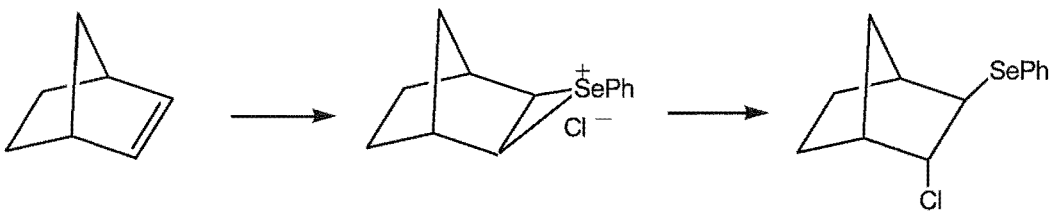
require a high degree of electron deficiency at C2 if they were to play a role. It is unclear as to whether there would be significant interaction between C2 and C6 if this deficiency is lower. This thesis sets out to examine whether there is any evidence for interactions between these two carbons when the electron deficiency at C2 is relatively low. Three approaches are used.

In the first, the effect of a substituent X on the ^{13}C NMR chemical shifts of the alkenic carbons in a 5-X- 2-norbornene is examined. In the absence of significant direct interaction between C5 and C3 the main factor that should influence the chemical shifts of these should be the polar effect of X. The extent to which the shifts depend on whether X occupies an *exo* or *endo* position will also be considered. If the polar effect influences the shifts mainly by an inductive mechanism this should not be important, but if the field effect of the C—X dipole is a major contributor, then significant differences between the two could be involved. On the other hand, if there *is* significant interaction between C5 and C3, then the possibility arises that in addition to the form of σ bridging interaction proposed by Grob, interaction between any lone pair or π system on X and the π orbital of the C=C bond may be possible, and this could also influence the chemical shifts.

In the second approach, the reaction of 5-X-substituted 2-norbornenes with phenylselenenyl chloride is investigated. Phenylselenenyl chloride reacts with the C=C bond of an alkene by essentially the same mechanism as molecular bromine. The addition takes place in two steps. In the first step the electrophilic portion of the reagent (PhSe) adds to form a cyclic intermediate (a phenylseleniranium ion). The ring is then cleaved by attack by the associated chloride ion to give the adduct. As with bromine, the addition takes place exclusively anti.

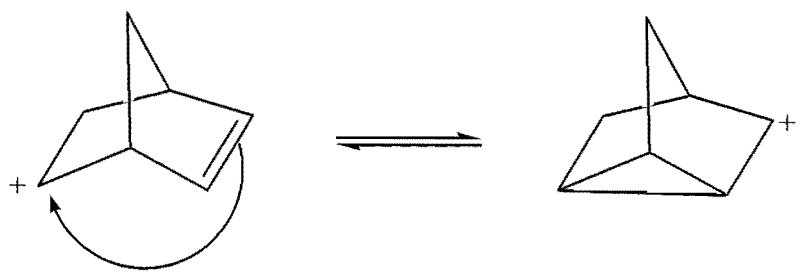


Seleniranium cations are stable enough to isolate, if associated with a non-nucleophilic anion (e.g. SbF_6^- or PF_6^-) and this suggests that most of the positive charge is carried by the selenium. When phenylselenenyl chloride adds to the double bond of 2-norbornene, the reagent attacks the less hindered *exo* face, and in the final product the phenylselanyl group is always *exo* and the chlorine always *endo*.



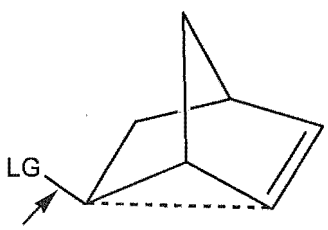
The exclusive *anti* stereochemistry of the addition strongly suggests that the reaction of chloride on the intermediate is an S_N2 process. If this is indeed the case, then the intermediate may be regarded as a norbornyl derivative in which there is some positive charge on C2, but not as much as on a 2-norbornyl cation. In such circumstances σ delocalisation is less likely. While only a single product forms from 2-norbornene itself, a 5-substituted 2-norbornene, being unsymmetrical, can form two isomeric *exo-endo* adducts, and it is of obvious interest to discover whether the relative yields of the two reflect solely the polar effect of the substituents, or whether σ delocalisation affects this.

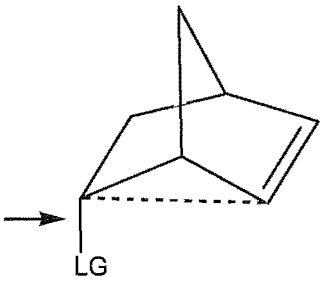
The third approach was based on direct measurements of bond lengths by X-ray diffraction. Generation of a positive charge on a 2-norbornenyl carbocation leads to it readily rearranging to a nortricyclyl one[5,6]:



A 5-X-substituted 2-norbornene in which X is a good leaving group might be expected to have the bond to C5-X bond polarised to such an extent that C5 develops a partial positive charge. In such circumstances there may be some

interaction between this carbon and the π system of the double bond. This could show up in the form of a lengthening of the C-X or C=C bond in such a molecule. Such a change in bond length could well be different when X was *exo* from when it was *endo*, and possibly be large enough for this to be observable.





A limited range of compounds with a selection of suitable leaving groups was prepared and their structures were determined by single crystal X-ray diffraction.

Chapter 2.

THE EFFECT OF SUBSTITUENTS ON THE ^{13}C NMR CHEMICAL SHIFTS OF THE sp^2 CARBONS OF 5-SUBSTITUTED 2-NORBORNENES

2.1 Introduction

The relationship between the structure of a molecule and its chemical reactivity has always been a topic of interest in chemistry, and has been the subject of much study over the years[7]. The general approach has been to study the effect of making a structural change on a reaction rate or the position of some equilibrium. The observed variation in the reactivity is the result of changes in the environment of the molecule around the part of the molecule where the reaction is taking place. Such changes will involve the electron distribution in the vicinity and/or the spatial environment. The first is commonly referred to as the *electronic effect* and the second as the *steric effect*. The 'structural change' made usually involves the replacing of one group in a molecule by another, and the observed changes are usually, by convention, referenced to the molecular structure that has a hydrogen as the group replaced. If the group replaced lies in close proximity to the reaction site, both its steric effect and electronic effect may affect the reaction. However, if it lies some distance away, the change in the spatial environment in the region of the molecule where the reaction is occurring may well be negligible. In these circumstances only the electronic effect needs be considered, as this falls off with distance much less rapidly than the steric one. Of the two substituent effects, the electronic one is the more transferable from one system to another, and for this reason has been far more widely studied. Among its advantages are (a) the degree to which it is attenuated by structural factors such as the distance between the group and the reaction site is more predictable, (b) it is possible to have the group far enough away for steric effects to be negligible, but the

electronic effect to still be significant, and (c) its magnitude often tends to be constant and independent of the structure of the rest of the molecule.

If steric effects can be ignored, the group introduced (or 'substituent', as it is usually called) affects a chemical reaction by a combination of its intrinsic electronic effect and the efficiency with which this is relayed to the site in the molecule at which the reaction is occurring. The intrinsic electronic effect has two components. The first of these, the polar effect, is a unique property of the substituent, and is independent of the reaction that is taking place. Its magnitude is constant, but its effect on a reaction will vary according to the distance between it and the site in the molecule at which the reaction is occurring. The second, the resonance effect, is not constant. It arises whenever π electron delocalisation involving the substituent and other π systems in the molecule (which may or may not include those of the reaction site) occurs. In other words, it can vary, depending on the core structure of the molecule, and can also be reaction dependent. This is not as bad as it sounds. In many situations electron delocalisation is not possible, i.e. any lone pairs or π bonds on the substituent remain localised on the substituent, so the resonance effect will be zero. In others it may involve other parts of the molecule but not the reaction site, and be constant for that particular type of structure. Furthermore, even in cases where it can involve the reaction site, it frequently shows a tendency to have a constant magnitude.

2.2 The Quantification of Substituent Effects

2.2(i) The Hammett equation

The magnitude of the substituent effect of any group is a unique property of that group, and in any discussion of substituent effects its magnitude relative to that of other groups is of obvious interest. While it is not difficult to arrive at an order of their magnitudes, this is much less useful than a quantitative scale of these. The usefulness of such a scale was recognised immediately chemists started taking an interest in the systematic investigation of the effect of structure

on reactivity. The obvious approach was to relate the electronic effect of a substituent to its effect on either the rate constant or equilibrium constant for some standard reaction. Since methods were available for determining both of these accurately, comparison of the effect of a series of substituents on one of them could be used as a basis for assigning a relative numerical value to a substituent's electronic effect. Ideally, one would start by selecting as a standard reaction one in which both steric and resonance effects were negligible, and in the first instance derive a scale of polar effects, to which the resonance effect could subsequently be related by some means or other.

As it happens this approach was not adopted, for pragmatic reasons. An ideal reaction for the purpose would be one for which a large proportion of the required data was already available in the literature. Unfortunately, at the time during which interest was developing in this area (the late 1920s and early 1930s) there were no reactions that fulfilled these criteria and for which steric effects and π delocalisation were absent. However there was one reaction for which reliable data covering a wide range of substituents was available, and in which steric effects were absent — the dissociation constants of *meta-* and *para-X* substituted benzoic acids in water at 25°. A large number of these, measured with a high degree of precision, were available following an extensive study by Dippy and co-workers[8-10]. Unfortunately resonance effects in this reaction were not entirely absent, even for the *meta*-substituted ones, but for most, especially the latter, they were constant. The electronic effect of a substituent X in this reaction was designated the *substituent constant,* given the symbol σ and defined as

$$\sigma \equiv \log K^X/K^H$$

where K^X is the dissociation constant of the *meta-* or *para*-X-substituted benzoic acid and K^H that of benzoic acid, both measured in water at 25° C. This meant that each substituent X had two values of σ, one for when it was *meta-* to the carboxyl group and one when it was *para* to it. It turned out that the resonance contribution to σ when X is *meta* to the reaction site in a benzenoid system is independent of the reaction, so that for any reaction of any *meta*-X-

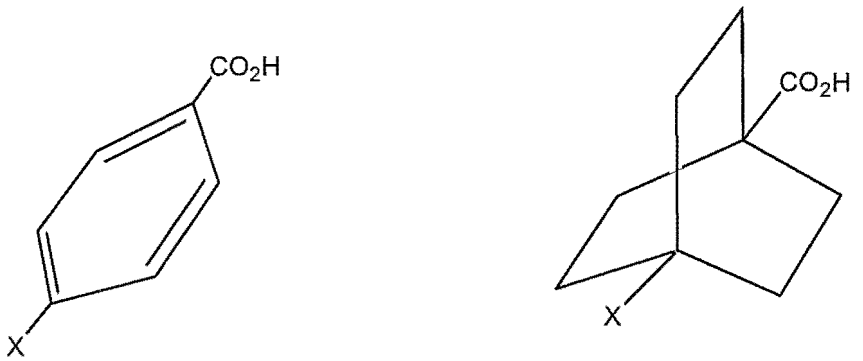
substituted benzene derivative there exists a linear relationship between the logarithm of the equilibrium constant or rate constant and the σ^{meta} value of X. This relationship could be expressed in the form

$$\log K^X/K^H \text{ (or } \log k^X/k^H) \quad = \quad \rho\sigma$$

where ρ (known as the *reaction constant*), represented a measure of the sensitivity of the reaction to the electronic effect of the substituent. The equation is known as the *Hammett Equation*, and is named after L. P. Hammett who first proposed it[11]. The equation also applies for *para*- X substituents provided there is no significant direct resonance interaction between X and the reaction site. (The resonance contribution to σ^{para} is different from that to σ^{meta} but independent of the reaction in these circumstances.) If there is an interaction with the reaction site and this varied during the course of the reaction, then the normal σ^{para} value no longer applied, and an alternative enhanced value had to be used instead. The most common situation where this was observed at the time was when the reaction site was a strong resonance donor such as an amino or hydroxyl group. When X was *para* to this and was a strong resonance withdrawing substituent, e.g. a nitro, acetyl, or cyano, a strong direct interaction between the two existed, and the resonance contribution to the σ value for that substituent was much greater than normal. Fortunately this enhanced σ value (commonly referred to as its σ^- value) proved to be virtually the same for most reactions of this type, which meant it could be used for all of them. If an enhanced σ^- value was needed for a good correlation to be observed, this could be used as evidence that such an interaction existed. The reverse situation also applied — when a strong resonance donating substituent was *para* to a strongly resonance withdrawing reaction site, the resonance donor could be assigned an alternative σ value (σ^+) for use in such situations. (In practice such reactions were much less frequently encountered.)

2.2 (ii) The Resolution of Electronic Effects

The previous approach applies well to many aromatic systems, because they (especially when X is *meta*) tend to have essentially constant resonance contributions that arise mostly from resonance interaction between the substituent and the aromatic nucleus. However the σ values derived in this way are composite ones – they still contain resonance contributions, and because of this cannot be used in situations where the resonance contribution to the electronic effect is zero. For such situations, one needs a set of σ values that represent solely the polar contribution of the substituent X. Setting up such a scale can be done by choosing a suitable standard reaction where neither steric nor resonance effects are involved, and measuring the necessary data. In this way the property being measured will respond only to the polar effect of X. The problem is how to relate such a scale of values obtained in this way, perhaps by means of a different standard reaction, to Hammett's original scale of σ values, since the ones obtained will not be equal to, but proportional to, the polar component of σ^{meta} and σ^{para}, and unlikely to be the same. The first person to create such a scale of polar substituent constants, R.W. Taft, made no attempt to align the scales.[12-15] However subsequently the two were brought into line with the help of data obtained by J. D. Roberts, who measured the dissociation constants of a limited range of 1-X-[2.2.2]bicyclooctane-4-carboxylic acids (**5**), and compared these with those of the corresponding benzoic acids under the same conditions[16]. In 1-X-[2.2.2]bicyclooctane-4-carboxylic acids the carbon skeleton is rigid, and the substituent X and the carboxyl group are not only in the same relative orientations, but also virtually the same distance apart as in the corresponding benzoic acids (see next page). In this system, any resonance interaction between X and either the saturated skeleton or the carboxyl group should be negligible. Consequently only the polar effect of X should affect the pK_a of the acids.



(5)

Since the orientation of the C-X bond is the same in the two systems, the magnitude of the polar effect of X depends on its distance from the reaction site (see following section), and this distance is the same in the two series, the two scales can be aligned. As the synthesis of 1-X-[2.2.2]bicyclooctane-4-carboxylic acids is difficult, only a limited number were prepared. However sufficient were made for a graph of Taft's earlier polar substituent constants (which he referred to as σ^* values) against pK_a to be obtained, and by comparing the slope of this with the reaction constant for the ionisation of benzoic acids under the same conditions, a quantitative relationship between the two scales could be established, and a scale of polar substituent constants (σ_I values) that corresponded quantitatively to the polar contributions to Hammett's σ values derived. Since this time a number of other reactions involving other systems where electron delocalisation is not possible have been studied, and the validity of Taft's values confirmed. There are occasional discrepancies observed, but these are usually minor.

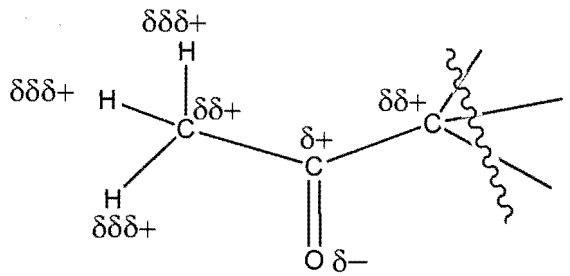
2.3 The origin and nature of polar effects.

The polar effect is a consequence of the unequal sharing of bonding electrons in the substituent that arises when atoms with differing attractions for electrons are bonded to one another. In organic molecules, usually one of these is a carbon, and the other either another carbon in a different environment or another element. The most commonly encountered 'other elements' are N, O, or a halogen. The asymmetric sharing of electrons that results giving rise to a dipole, and it is this dipole that is considered responsible for the polar effect. The

electrons shared may be in either a sigma bonding orbital or a π one, and since π electrons are less tightly held, their orbitals are more easily distorted, so the magnitude of the dipole, and hence the polar effect that results from π orbital polarisation, is greater than that from the sigma ones between the same atoms. It is customary to define a 'substituent' as a group attached to the core skeleton of a molecule, the assumption being that it substitutes for a hydrogen in the 'parent' compound. In only a few cases does the 'substituent' consist of a single dipole. The simplest situation would be where the carbon of the skeleton to which substituent is attached forms one end of the dipole and some other atom the other. For a hydrogen to be replaced by the atom of another element the latter must necessarily be either univalent or else bear a charge. The only neutral substituents in this category are the four halogens. However –CN could almost be considered to fall into it, as the C≡N bond is sufficiently short relative to C—C one that C—C≡N could almost be considered to represent a single dipole. In all of these cases the carbon atom constitutes the positive end of the dipole. In fact, because carbon is a relatively electropositive element, in most organic compounds it is the positive end of the dipole.

Normally there is more than one dipole present in the substituent. However, often some are very weak and can be ignored. Bonds between atoms of similar electronegativity (e.g. C—H or C—C bonds involving carbons in slightly different environments), may contribute little to the overall dipole of a substituent, if there is another present where the electronegativity difference involved is large. Such multi-atom substituents may give rise to, not only a dipole in which the carbon of the molecule to which they are attached forms one end, but also to individual dipoles in which this carbon is not directly involved. For instance, consider the situation where the substituent is an acetyl (CH_3CO—) group. There will be present three C-H dipoles, one C-O dipole containing contributions from both the sigma and π bonds, and two C-C dipoles, one between the CO and the CH_3, and the other between the CO and the carbon on the core of the molecule to which it is attached. Although the system is apparently a very complicated one, the main dipole contributing is that due to the C-O sigma and π bonds. In this dipole the oxygen forms the negative end and the carbon the positive one.

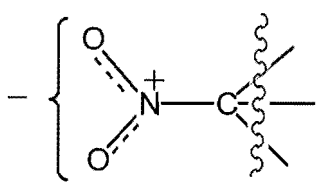
However its presence induces others. For example, it carries sufficient positive charge on the carbonyl carbon for this to attract electrons towards it from the other two carbons to which it is linked. As a consequence, both of these will acquire partial positive charges. This process will be repeated by these carbons so that while, in the substituent as a whole, the negative end of the dipole will be the oxygen, the positive end will be more diffuse (**6**).



(6)

There are two further points that are relevant when considering the overall polar effect of a substituent such as acetyl. One is that, although the positive charge on the carbonyl carbon is of greater magnitude than the others, the carbon on the molecule to which it is attached is closer to the reaction site. This means that although it is less positive, its effect will be enhanced because the efficiency with which this is relayed to the reaction site falls off with distance. The second is that the position of the dipole is not fixed, as the substituent is free to rotate around the C—CO bond. It is entirely possible that the magnitude of its effect on the reaction site may depend on its orientation. If it can freely rotate, the polar effect will depend on its average position.

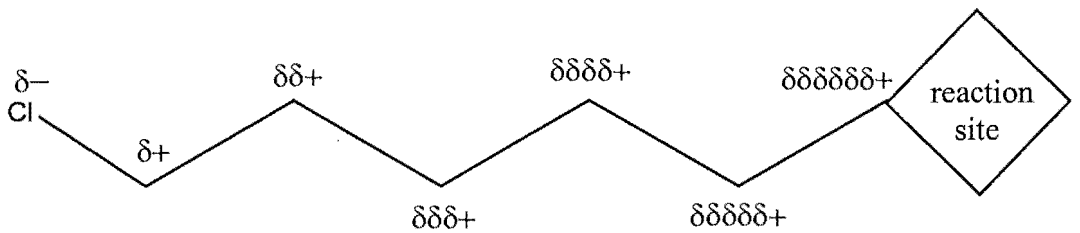
Some substituents are even more complicated. For example the nitro group contains three strongly electronegative groups, with two N-O bonds of equal bond order at an angle of ca. 120° to one another(7), and the whole linked to the molecule via a strongly electropositive N.



(7)

2.4 The Transmission of Polar effects

While there is general agreement as to the origin of polar effects, there is less as to how these are relayed from the substituent to the reaction site. There is however, agreement that two pathways are potentially involved. The problem lies in deciding which is the more important. The one originally proposed basically assumed that the polar effect is relayed from the substituent to the reaction site through the bonds of the molecule by successive induced polarisation of these. It assumes that polarisation of the type illustrated for the acetyl group on the previous page successively continues through the molecular skeleton (**8**) until it eventually reaches the reaction site, e.g. for a Cl substituent,



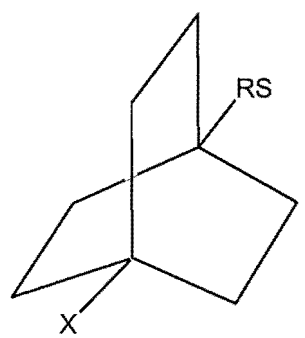
(**8**)

This interpretation was first put forward by Lewis, and subsequently taken up by Ingold[17]. Because of its mode of operation it was known as the *inductive effect*. Subsequently, an alternative view was put forward that the polar effect of a substituent influenced the reaction site by virtue of the field effect of the substituent dipole[18]. In other words, rather than being relayed through the intervening bonds, it was transmitted through space. This effect is commonly referred to as the *field effect* or *electrical effect*. One of the problems in distinguishing between the two is that the majority of reactions are carried out in solution, often in solvents of relatively high dielectric constant such as water or the lower alcohols. This means that the medium of lowest dielectric constant is often the body of the molecule, and therefore the lines of force pass through this.

It was noted previously that the effectiveness of transmission of the polar effect from the substituent to the reaction site depended on the distance between the two. If the body of the molecule is relatively flexible then this distance can

vary considerably. A particular problem is that if both the substituent and the reaction site are dipolar, they may be attracted to one another, with the result that steric effects will re-enter the picture. Regardless of whether or not this happens, the average distance between the two is capable of varying, as will the average orientation of the dipole. However since the inductive effect passes through bonds, it should be less sensitive than the field effect to the distance between the substituent and the reaction site, so that the relative contributions of the two types of effect will not remain constant. In addition, any substantial change in distance will certainly be accompanied by a change in the orientation of the dipole.

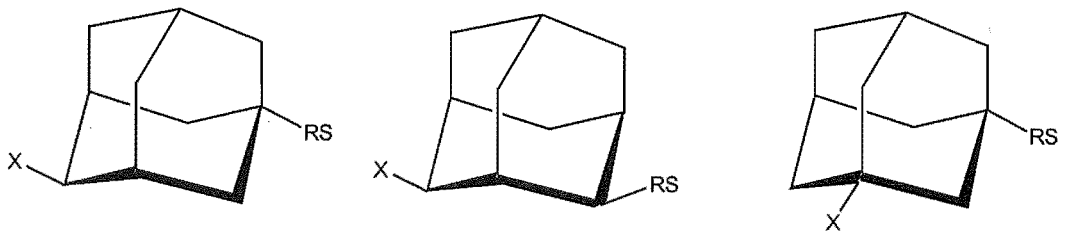
For these reasons, investigations of polar effects are usually based around molecules in which the molecular skeleton is rigid. In this way the substituent and reaction site remain a fixed distance apart, and as far as the substituent is concerned, at least the bond between it and the carbon skeleton maintains a fixed orientation (although individual dipoles within the substituent may not). The most widely used framework has been based on [2.2.2]bicyclooctane (**9**), with the substituent and reaction site bonded to the 1- and 4-positions



(**9**)

The advantage of such a system is that the 1- and 4-carbons are virtually the same distance apart as the 1-and 4-carbons of a benzene ring, and substituents on these would bear the same relationship to one another as they would in a *para*-disubstituted benzene.

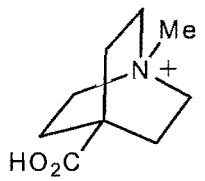
More recently the adamantane[19,20] skeleton (**10**) has received attention as an alternative, its advantage being that it can be used to represent a sterically rigid cyclohexane system.



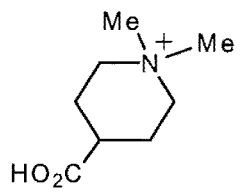
(10)

However, as with the bicyclooctane[21] systems, synthesis of the necessary compounds for study can be difficult, and this has limited its use.

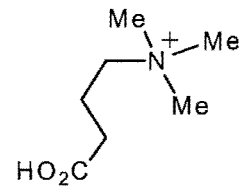
In both of these types of system the distance and the number of bonds between the two are kept constant, so that the relative importances of the field effect and the electrostatic effect should remain the same. However there have been a number of efforts to construct systems that could be used to investigate the relative importances of each. A summary of the current situation is to be found in a review by Bowden and Grubbs[22]. One approach was to try to keep the distance between the reaction site and the substituent the same but to vary the number of links. For example, Grob[23] measured the pK_a's of a number of betaines(**11**) where the same linking groups were involved, but the number of them different. He compared these with the values for the corresponding parent acids. After correction for steric effects, he found the effect of the additional bridging was relatively small and incompatible with the through-bond inductive effect representing an important transmission pathway



ΔpKa =2.03



ΔpKa =1.57



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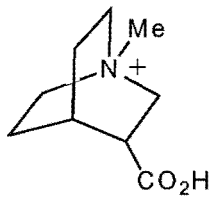

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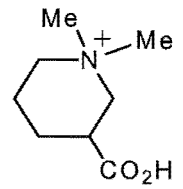

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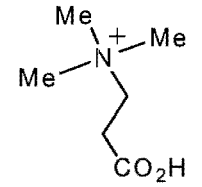
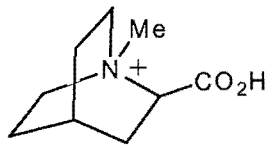
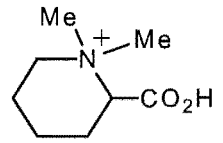


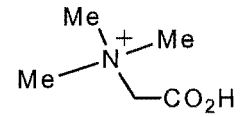
ΔpKa =1.96



ΔpKa =3.89



ΔpKa =3.75

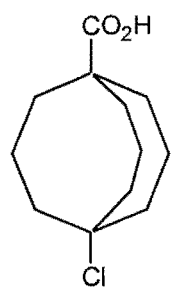


ΔpKa =3.44

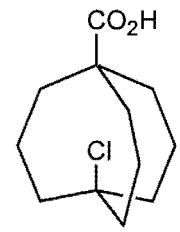
(11)

Similar studies on the transmission of polar effects in the ionisation of the 1-X-4-cyclohexanecarboxylic acids, 1-X-4-[2.2.2]bicyclooctanecarboxylic acids, and 1-X-4[2.2.2]bicycloheptanecarboxylic acids supported Grob's conclusions[24].

An alternative approach is to modify the field effect of the substituent dipole by deliberately changing its orientation. As long ago as 1955 Roberts[25] suggested that the ideal way of distinguishing the two possibilities would be by comparing the dissociation constants of (**12**) because the C-Cl dipole is reversed in the second molecule.

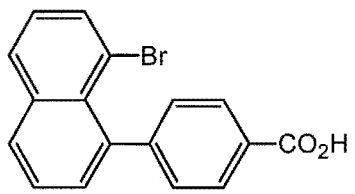


and



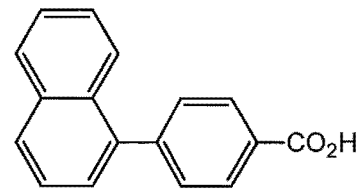
(12)

However there would obviously be real synthetic problems involved in making the second compound and, unsurprisingly, it has never been synthesised. There have, however, been instances where more accessible variants based on the same principle have been prepared. For example, in 1,8-disubstituted naphthalenes, the dipoles of the substituents are oppositely oriented to those of their 1,4 or 1,5-analogues. Bowden and Ghadir[26,27] measured the pK_a values of 4-(8-bromo-1-naphthyl)benzoic acid (**13**) and 4-(1-naphthyl)benzoic acid (**14**) and found that the bromo acid was weaker than non-bromo one.



$pK_a = 7.09$

(13)



$pK_a = 6.60$

(14)

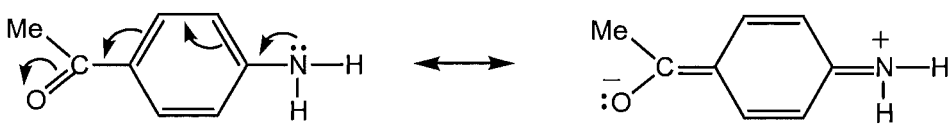
In contrast, 4-bromobenzoic acid is about 0.5 pK units *stronger* than benzoic acid. It is unlikely that the presence of the bromine in the 8-position of the naphthalene ring would have a significant steric effect on the loss of a proton from the carboxyl group, so the result is consistent with the reverse orientation of the C—Br dipole leading to a reversal of the substituent's polar effect. Similar trends were also observed by Bowden and Hojatti[28] in 8-substituted -1-naphthylpropiolic acids. Studies in other systems where the orientation of the substituent dipole has been reversed support the above results[22].

Most of the evidence regarding the mechanism by which the polar effect of a substituent is relayed to a reaction site supports the field effect over the inductive effect as the major contributor to the total. The current position is summarised in three reviews by Marvin Charton, Otto Exner, and Vladimir Galkin published in 1999 in the *Journal of Physical Organic Chemistry*[29-32]. It is perhaps significant that there was not universal agreement between the authors, a fact that becomes obvious when one reads a separate comment at the end jointly written by them summarising the existing position. Charton favours the field effect, and by

invoking Occam's Razor, would discard the inductive effect altogether. In contrast, Exner believes that neither is, in principle, correct, while Galkin believes that it is better not to worry too much about understanding how the effect operates, but to concentrate on using it.

2.5 Resonance Effects

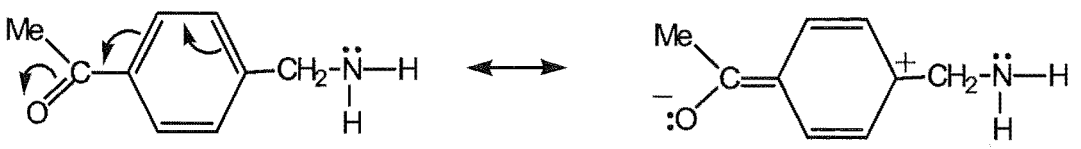
The polar effect is a localised one. In other words, it is generated on the substituent, by the substituent, and operates on the reaction site from a distance. It arises as a result of distortion of localised σ or π bonds, and the effect of the dipole generated is relayed to the reaction site either as a through-space field effect or by successive distortion of adjacent localised bonds. In contrast, the resonance effect is delocalised. Like the polar effect, it is a property of the substituent, but it is transmitted by overlap of p or π orbitals on the substituent with adjacent ones in the core of the molecule. Often this overlap may extend to include suitable orbitals on the reaction site. If this occurs, 'transmission' between the substituent and the reaction site has no real meaning, as the two are essentially part of the same system. For example, consider the situation in 4-aminoacetophenone (assuming that the amino group is the reaction site and the acetyl group is the substituent. Delocalisation of the π system will lead to transfer of charge from the side chain to the reaction site. This can be conveniently shown by drawing the appropriate resonance form.



I **II**

Note that the real structure of the molecule will resemble to some extent both of these forms, so the total substituent effect will consist of a polar contribution from the CH_3CO group in **I** that is relayed by a field/inductive effect, together with a resonance contribution due to **II**. If the resonance interaction only

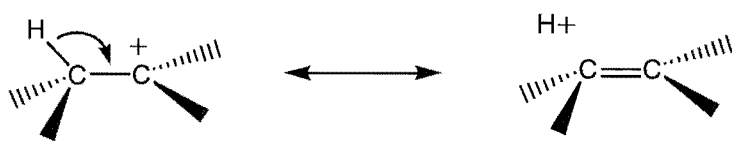
extends part of the way, its contribution to the total substituent effect will be much lower, e.g. (**15**)



(**15**)

Here, because the positive charge must be carried by the ring carbon rather than the nitrogen of the amino group, the former will only have six electrons in its outer shell. This decreases the contribution of the resonance form from what it was in **II,** but does not eliminate it altogether. Resonance effects therefore tend to be greatest when the substituent and reaction site can interact strongly.

Strong resonance interaction between a substituent and the reaction site requires that the two be linked by a conjugated π system, so that adjacent π orbitals can overlap efficiently. This would seem to rule out resonance effects as a contributor to substituent effects in a saturated system. However there are circumstances where resonance effects of a different type can become involved. The traditional resonance effect involves the overlap of p (usually 2p) or π orbitals with adjacent p or π orbitals. However in appropriate circumstances it is possible for σ bonds to overlap significantly with adjacent p orbitals. The 'appropriate circumstances' requires that the adjacent orbitals being overlapped be either a vacant 2p one, or a π one that is sufficiently polarised for it to behave as if it were vacant. This is because σ bonds are usually poor electron donors. The best known example of resonance of this type is the phenomenon of *hyperconjugation*. It is most commonly encountered in the form of C—H hyperconjugation, where a C—H bond acts as the equivalent of a lone pair to stabilise an adjacent cationic carbon.

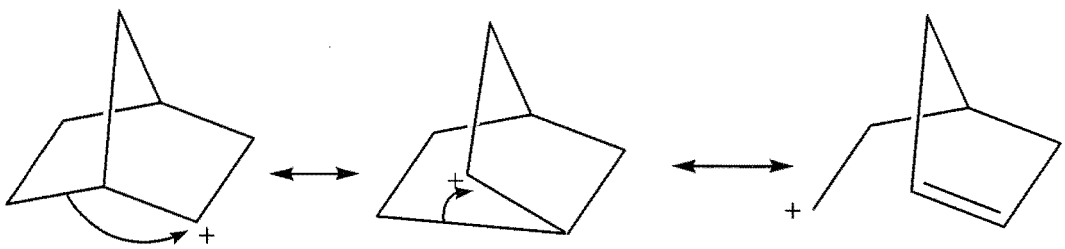


(**16**)

Hyperconjugation as illustrated in (**16**)[33,34] is responsible for the order of stability of simple aliphatic carbocations being

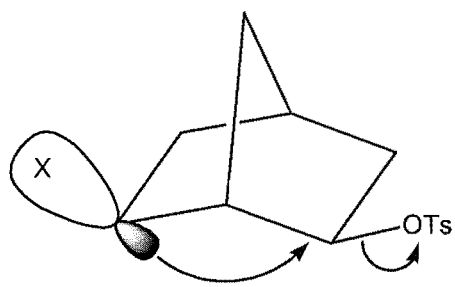
tertiary > secondary > primary > methyl

and for the methyl group of toluene activating the nucleus towards electrophilic attack much more than would be predicted on the basis of the polar effect of a methyl group. However hyperconjugation would not be expected to represent a major mechanism for the transmission of substituent effects in the absence of a very strong electron demand of the type present in carbocationic species. C—C hyperconjugation is also known, but is less commonly encountered. The 2-norbornyl cation (**17**) could be regarded as an example where this is observed.



(**17**)

Another form of σ bond overlap with a vacant p orbital involves bonds, not on an adjacent carbon, but on the one adjacent to that. This phenomenon is known as *homoconjugation*. In this interaction the back lobe of a σ bond, if suitably oriented, overlaps with a vacant (or incipiently vacant) p orbital. Such an interaction was postulated by Grob to explain the ability of a 6-*exo*- substituent to apparently anchimerically assist the solvolysis of a 2-*exo*-norbornyl tosylate[4] (**18**)



(**18**)

Some of Grob's work is discussed later in this thesis (page 93). As with hyperconjugation, however, transmission of a substituent effect by this mechanism is most likely to be important only when significant electron deficiency at a reaction site is involved, and becomes much less likely as the distance between the substituent and the site increases.

On the whole it has rarely proved necessary to invoke the phenomena of hyperconjugation and homoconjugation to explain the relay of substituent effects through saturated carbon skeletons to reaction sites and in cases where it is, the evidence supporting it is not always strong.

2.6 The Effect of Substituents on NMR chemical shifts.

One of the main problems encountered in the quantitative interpretation of the effect of substituents on reactivity in organic compounds has been the disproportionate amount of the time required to be spent on the acquisition of data. This is because interpretations are based on correlations of data obtained for a number of substituents, and the greater the number, the more reliable the interpretation. Initially, reactivity data were based on the measurement of reaction rates or the positions of chemical equilibria (mostly ionisation constants of acids and bases or rates of ester hydrolysis), and even ignoring the problem of obtaining the desired compounds, the time taken to make the necessary measurements far outweighed the time taken to interpret them. Early investigators in the field (e.g. L.P. Hammett) were able to shortcut the process by making use of reliable data existing in the literature that had been obtained by other workers for a different purpose. However it did not take long for the point to be reached where investigators found it necessary to devote time and resources to producing their own compounds and obtaining their own data. While designing appropriate structures for study was not difficult, making the specific compounds based on these could be time consuming, and making the measurements certainly was. Little could be done about the first of these problems, but the second could be overcome if a reaction could be found from which reliable data of high precision could be obtained quickly. Initially no such reaction could be found — usually a

trade off between speed of acquisition and reliability was involved. The most obvious answer lay in spectroscopy. With suitable instrumentation, measurements could be made both accurately and quickly. Suitable instrumentation started to become commercially available from the 1950s onwards. In the Chapman and Shorter's review volume "Advances in Linear Free Energy Relationships" that appeared in 1972, there were chapters on the use of optical spectroscopy (IR and UV) and on nuclear magnetic resonance (^{1}H, ^{19}F, and ^{13}C)[35,36]. It is interesting to note that the NMR review devoted only 2 of its 58 pages to ^{13}C NMR and four to ^{19}F. A second volume ("Correlation Analysis in Chemistry"), by the same editors, and considered by them to be an update, appeared six years later[37]. This had a 40 page chapter on nuclear magnetic resonance, and the bulk of the work involved ^{13}C shifts. It was no coincidence that (relatively) cheap FT-based commercial instruments giving ^{13}C NMR spectra based on natural abundance had become widely available during the interim.

Investigation showed that ^{19}F and ^{13}C chemical shift measurements were the most promising probes. Neither was perfect, in that the observed effect of a substituent on a chemical shift did not appear to reflect solely the electronic effect of the substituent, but it was possible to devise systems where it came acceptably close to doing so. Of the two, ^{13}C chemical shifts appeared the more useful, in that excellent data could be obtained using compounds with ^{13}C at natural abundance levels, and this considerably simplified the problem of their synthesis. In addition, chemical shift data on all carbons present in the molecule could be obtained in a single measurement, allowing the investigation of the effect of a substituent on the shift for any of the carbons present in the spectrum. For ^{19}F NMR the early advantage of the 100% natural abundance was lost, while the synthetic problems remained. Today most investigations in this area involve the ^{13}C nucleus. (A search of SciFinder under the topics *^{19}F NMR substituent effect* and *^{13}C NMR substituent effect* yielded ca 200 and 1500 references, respectively.) However the ready availability of multinuclear facilities has led to increasing interest in exploring other nuclei as probes of substituent effects. Unfortunately ^{1}H chemical shifts have not proved particularly useful, and since ^{13}C shifts can be readily obtained for the same compounds, these currently receive more attention.

I will confine further discussion of the influence of substituents on NMR chemical shifts to their effect on ^{13}C ones, since these are the only ones I will be concerned with in this thesis.

2.7 The Effect of Substituents on ^{13}C NMR Chemical Shifts

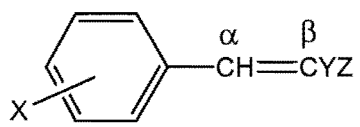
As with reactivity studies of substituent effects, much of the early work on correlating ^{13}C NMR chemical shifts with the substituents present in the molecule was carried out on aromatic systems, because of their ready availability and the simplifying effect of their rigid structures. It is generally accepted that the effect of a substituent on the rate of a reaction or the position of equilibrium is related to changes in the electron density at the reaction site, and that this responds to changes in the substituent. There is considerable evidence that the positions of ^{13}C NMR chemical shifts also respond to changes in electron density at the probe site, and these are usually sufficiently substituent sensitive to be easily measured. However attempts to quantitatively correlate the effects of these with the polar and resonance effects of substituents have met with only limited success because it became apparent quite early on that while the electronic effect of a substituent contributed to the observed chemical shift, it was not the only contributor, and in many cases other "non-electronic" factors could be important. One important difference from a quantitative point of view is that the relative sensitivities of the shifts to polar and resonance effects is not the same as that observed in chemical reactions. In the latter, in aromatic systems at least, the relative efficiencies of transmission of the two are either the same, or else that of resonance effects is zero. In the case of ^{13}C chemical shifts, on the other hand, while the transmission of resonance effects may in some cases be the same as polar ones, or zero (in saturated systems), they may also be non-zero but not the same as those for polar ones. In fact in some systems resonance effects may be relayed through the molecule much more efficiently than polar ones. One result is that most approaches to the quantitative correlation of ^{13}C chemical shifts with the electronic effect of substituents have involved analysing it by means of Ehrenson[38], Brownlee, and Taft's Dual Substituent Parameter equation[12].

$$SCS(X) = \rho_I\sigma_I + \rho_R\sigma_R$$

In this, SCS(X) is the substituent-induced chemical shift, i.e the change in chemical shift that is observed when a hydrogen in the parent molecule is replaced by X and σ_I and σ_R are values for polar and resonance substituent constants proposed by these authors.

In saturated systems ρ_R would be expected to be either zero, or close to it. On the other hand, in some aromatic systems, it can be quite high, e.g. for the *para* ring carbon in monsubstituted benzenes[15], ρ_R is about five times the magnitude of ρ_I. One of the consequences of using ^{13}C chemical shifts as a probe is that the data are sufficiently precise to show that if one takes into consideration the precision with which the substituent constant values are known, and that of the data, the correlations, although acceptable, are often not as good as they should be. This is best interpreted as indicating that the shifts were being affected to at least some degree by factors other than polar and resonance effects.

One system where, as with reactivity data, $\rho_I \approx \rho_R$, turned out to be the effect of *meta* and *para* substituents on the ^{13}C chemical shifts of the β-carbon of styrenes and their β-substituted analogues (**19**)[39,40]



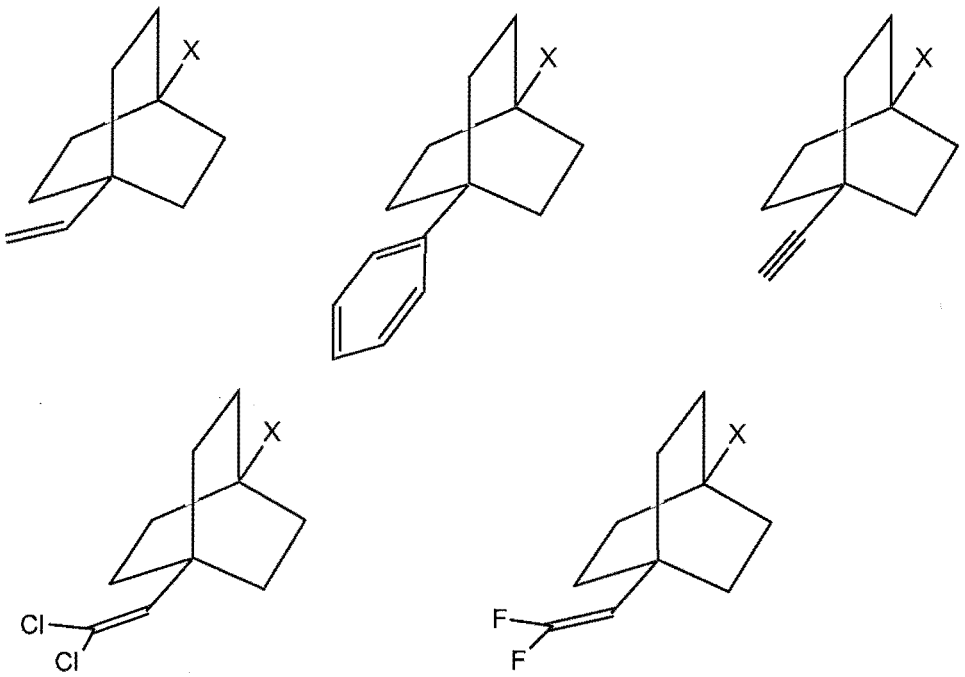
(19)

In these series not only was $\rho^{meta} \approx \rho^{para}$, but in the *para* series, the extent of interaction between the substituent (X) and the β carbon varied with the electronic character of Y and Z, being greatest when both were strong resonance withdrawers and X was a resonance donor. In addition, the correlation of the shifts with σ was sufficiently close as to indicate that the shifts were not being affected significantly by non-electronic factors. Attempts to correlate the shifts for the α carbon were much less successful. It was observed, however, that

whereas an electron withdrawing X tended to reduce the electron density on the β carbon, it tended to raise it on the α one. This suggested that the main effect of such a *meta* or *para* ring substituent on the electron density on the β carbon was the result of a localised polarisation of the double bond of the side chain. That, in spite of this, ρ_R was about the same as ρ_I in such circumstances was unexpected, and not easily explained.

In the light of the above results, there seemed no reason to believe that in a molecule with a structure that did not allow the transmission of resonance effects from the substituent to the reaction site, an ethenyl (or similar) group might respond in the same way to polar effects, and correlations might be obtained with polar substituent constants.

The main difficulty with investigating this is that elimination of resonance effects requires the use of a saturated carbon skeleton, and, as noted earlier, in order to eliminate the potential problem of steric effects, this should have a rigid structure, preferably one in which the relative orientations of the substituent dipole and the ethenyl group do not change. If the latter is free to rotate, their relative orientations will change, even if that of the substituent dipole does not. In practice, however, this might not matter, as rotation would be rapid, and the β carbon would occupy an average position. Unfortunately, using a vinyl group as a probe in such systems raises again the problem of synthesis. Preparing suitable compounds for study based on a rigid alicyclic system is not easy. Nevertheless Adcock and co-workers[21] prepared a limited range (H, Me, Ph, OMe, Br, and F) of 1-X-4-vinyl-[2.2.2]bicyclooctanes, and examined quantitative correlations with the polar effect of these substituents. He also studied some related bicyclooctanes (see below) using a greater range of substituents (**20**):



(20)

In each case he considered correlations involving both the α and β carbons (or C_{ipso} and C_{para} for the 4-phenyl series.) Correlations were acceptable, but on close examination they did not fit the data to within the normally accepted error limits for substituent constants.

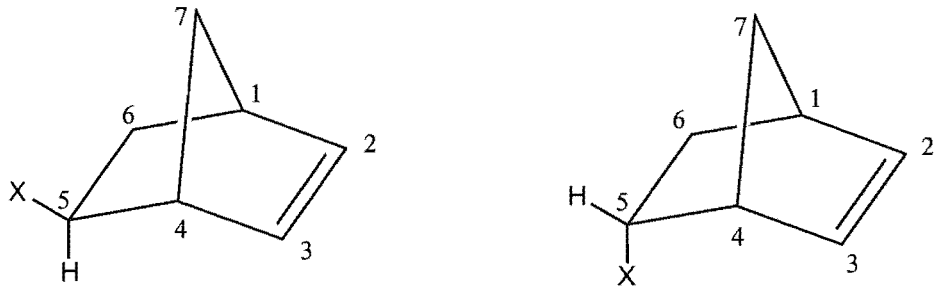
For the more common substituents, Hammett σ^{meta} values are considered reliable to within ±0.03 or better. However there is less agreement as to the values of the polar contributions to these (σ_I). The most widely used set of values is that proposed by Ehrenson, Brownlee and Taft for use in their Dual Substituent Parameter equation[15]. Their source is not entirely clear, but they appear to be based mostly on those derived by Taft earlier from reactivity data on aliphatic compounds and scaled to match the presumed polar contribution to Hammett σ_I values. Unfortunately a problem arises when these are used to correlate spectroscopic data such as ^{13}C NMR chemical shifts, as measurements of these are normally made using dilute solutions in non-polar solvents, whereas Taft's σ_Is are likely to have been mainly based on reactions carried out in hydroxylic ones such as water or alcohols. For the more dipolar substituents, especially ones that can

take part in hydrogen bonding in hydroxylic solvents, σ_I values derived from data obtained in water or alcohol solvent may not be appropriate for use in solvents such as $CDCl_3$, the most commonly used solvent for ^{13}C NMR studies. At least two sets of values considered appropriate for $CDCl_3$ have been proposed[39,41]. If these values are reliable, then any deviations should be due to contributions to the shifts from sources other than the polar effect of substituents.

If σ_I values appropriate for $CDCl_3$ are used to correlate Adcock's data, there are discrepancies. Most are minor — not large enough for one to unequivocally assign them to non-electronic factors. Further discussion of Adcock's results will be deferred until my results for the 5-substituted norbornenes are discussed.

2.8 The Effect of Substituents on the ^{13}C NMR Chemical Shifts for C2 and C3 in 5-X-2-Norbornenes.

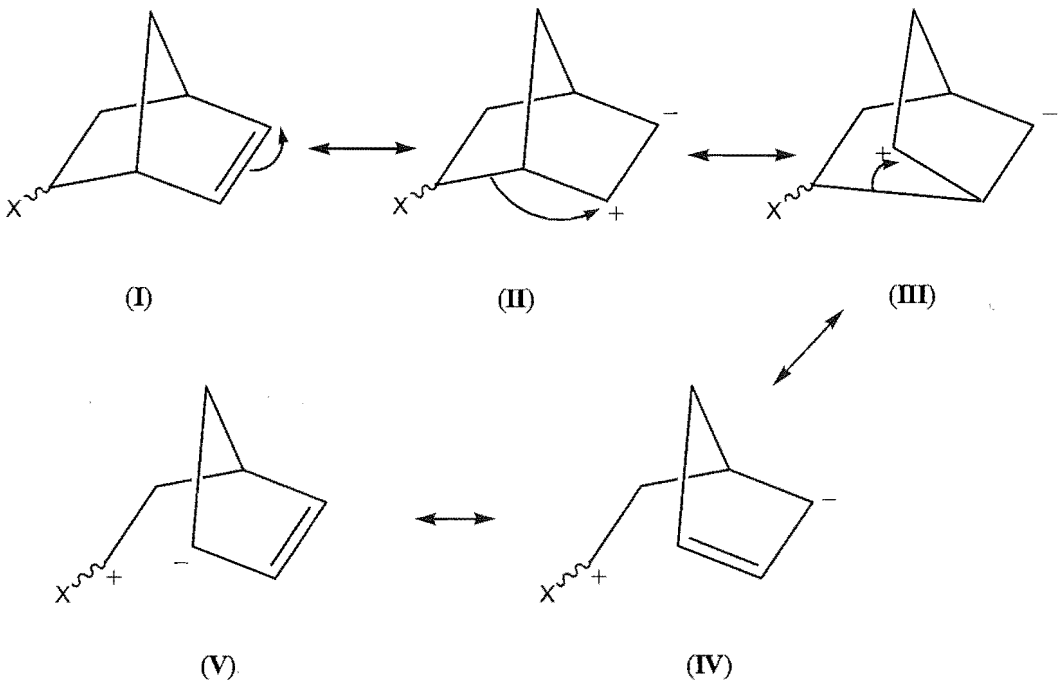
Adcock's results in the bicyclooctane series showed that ^{13}C NMR chemical shifts of the sp^2 carbon(s) of a C=C π system can serve as a probe for investigating the transmission of substituent effects through a saturated alicyclic system. The system chosen, with the substituent and probe occupying the 1- and 4-positions of [2.2.2]bicyclooctane was particularly well suited to minimise not only steric effects, but also the transmission of polar effects by pathways other than simple through-space or through-bond interactions. In addition, the C-X dipole is aligned more or less parallel to that of the probe (exactly so, in the case of -C≡C- and $-C_6H_5$) and the distance between the two is virtually identical to that in a *para* disubstituted benzene. However in the case of a 5-X-substituted-2-norbornene, the situation is not as simple. First of all, while the substituent X maintains a fixed orientation with respect to the norbornyl skeleton (**21**) at all times, there are two positions it can occupy, *exo* or *endo*. The two positions are not interconvertible in normal circumstances, so that for each substituent two isomeric structures exist.



exo endo

(21)

This means that two series of compounds are available for study. There is a potential for complications arising when X occupies an *endo* position, because its steric effect may not be negligible in this case, as the distance between it and the π system on the C3 carbon is not great. This would be especially true if X was large. In such circumstances proximity effects may become an issue. The best way to handle this problem would to confine any investigation to the *exo* isomers. Unfortunately this leads to loss of one aspect of the system that is potentially of considerable interest — the effect of the orientation of the C-X bond on the shifts of the alkenic carbons. A second potential problem arising from the framework structure is also basically a proximity one. It is a well established fact that in circumstances where C3 becomes even partly electron deficient, some degree of direct bonding between C5 and C3 becomes a possibility. If this is significant, then it could lead to the C3-C5 distance varying with X, which will in turn introduce a dependence of the transmission of the polar effect X. Such an effect is likely to be small. Of more importance, however is that the existence of C3-C5 bonding would result in additional mechanisms of electron transfer such as electron delocalisation becoming involved. Contributions arising from a number of resonance forms may be involved (see **(22)**).



(22)

Consideration of the resonance forms **(I)**–**(V)** above shows that while the one making the main contribution is undoubtedly **(I)**, any contributions from **(II)**-**(V)** will influence the electron densities at both C2 and C3, and as a result their ^{13}C NMR chemical shifts will be affected. In particular, any contribution **(IV)** makes should be very sensitive to the electronic effect of X, and if it is a resonance donor, this could lead to the shifts being sensitive not only to the polar effect of X, but also its resonance effect.

Common sense would say that resonance forms **(II)**-**(V)** all involve charge separation, and in the cases of **(II)**-**(IV)** also require that C2 carry a negative charge. As a result such contributions to the structure should be minimal. While this may be true, it should be pointed out that, even very minor contributions may still have a substantial effect on the NMR shifts. For example, in the *para*-substituted styrenes and β,β-dimethylstyrenes, there is clear evidence that the resonance effect of both +M and –M *para* substituents can have quite substantial effects on the shift of the β-carbon of the side chain, even though this would involve a resonance form in which that carbon bore a negative charge.

There is also another means by which anomalous effects might be introduced into such a system. (This was mentioned earlier in Chapter 1.) Grob[4] has proposed that if C3 becomes electron deficient, then C5 lies sufficiently close to C3 for the back orbital of C3 and any *exo* C-X bond to overlap significantly with C3, thereby introducing an alternative mechanism by which the transmission of the polar effect of X may be relayed to the probe site. However, as with the above, this should only become significant if C3 has an orbital available for the C-X bond to interact with, so it might not prove a major factor. However, as has been pointed out, ^{13}C NMR shifts of β-ethenyl carbons can be much more sensitive to small changes in electron density than one might expect. More importantly, overlap of this type is not possible when the substituent X occupies the *endo* position, since its back lobe will not be suitably oriented for this to be significant. This could lead to substantial differences in the efficiencies of transmission of electronic effects in the two systems.

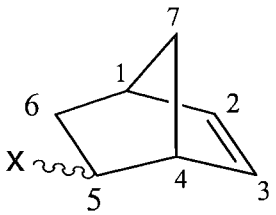
An investigation of the effect of 5-X substituents on the ^{13}C NMR spectra of 2-norbornenes is therefore well worth undertaking, as, if correlations are comparable to those of Adcock in the bicyclooctanes, this would demonstrate that these other factors are negligible. On the other hand, if anomalous results are obtained, it may tell us something about what sort of interactions are occurring within the framework that give rise to these.

2.9 Results and Discussion

In addition to 2-norbornene itself, a total of twenty two 5-X-2-norbornenes were prepared. Fourteen of these had the substituent in the *exo* position and nine in the *endo* one. The missing ones in the *endo* series were mostly those that could not be readily prepared using the equipment available. Unfortunately these included the chloro, bromo, and iodo derivatives, which would have proved particularly useful. (As –I, +M) groups they would have been helpful in assessing the relative contributions of these two effects to the shifts.) Since the study is concerned with substituent effects, we are concerned primarily with the position of the chemical shift relative to that of the same carbon in 2-norbornene itself. This difference is commonly referred to as the *Substituent Chemical Shift* and abbreviated as SCS.

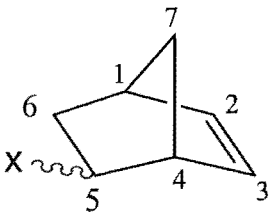
2-Norbornene possesses a plane of symmetry, so that for the shifts for C2 and C3 will be the same. In the 5-X compounds, however, as a result of polarisation of the double bond due to the electronic effect of the substituent, the two should differ. Since almost all of the substituents covered are electron withdrawing by a polar mechanism, as a result of induced polarisation of the π bond, the shifts for C2 of these would be expected to lie downfield of that for 2-norbornene, while those for C3 should lie upfield. However this represents an ideal situation and if substituent-dependent changes in the mechanism of transmission become involved, then this pattern might not be followed. The ^{13}C NMR chemical shifts of the norbornenes synthesised are given in Table 1 (see next page). For convenience the shifts for C2 and C3 of the 5-*X*-norbornenes are listed in the form of their SCS values in Table 2 following.

Table 1 ^{13}C NMR chemical shifts of 5-X-substituted-2-norbornenes



Substituent	C_1	C_2	C_3	C_4	C_5	C_6	C_7	other
H	41.73	135.28	135.28	41.73	24.57	24.57	48.49	
5-exo-cyano	41.75	138.06	133.96	47.36	27.13	32.12	47.09	123.55
5-exo-chloro	41.62	140.31	133.25	51.36	65.24	45.93	38.14	
5-exo-bromo	42.14	139.80	133.27	49.18	51.68	46.18	38.25	
5-exo-iodo	42.94	138.05	133.43	52.80	24.30	46.25	39.14	
5-exo-acetyl	41.66	138.23	135.78	45.34	51.68	29.02	45.93	210.73, 29.84
5-exo-carbomethoxy	42.96	138.04	135.72	46.55	41.61	30.32	46.34	176.74, 51.70
5-exo-amino	41.47	138.06	134.99	50.71	51.85	44.82	36.86	
5-exo-hydroxy	40.62	140.19	133.29	50.08	72.44	37.01	45.45	
5-exo-phenyl	42.77	137.33	137.27	48.17	43.68	33.65	45.73	
5-exo-methoxy	40.30	140.59	133.10	45.82	82.00	45.82	34.16	56.72
5- exo-acetoxy	40.55	140.99	132.55	47.19	75.17	46.15	34.52	21.37, 171.14
5-exo-hydroxymethyl	41.53	137.32	132.08	42.12	49.43	28.70	43.48	66.30
5-exo-isocyanato	46.17	140.25	132.75	55.31	49.81	41.06	35.62	
5-exo-carboxyl	41.64	138.07	135.66	46.90	43.42	30.30	46.37	182.81
5-endo-cyano	42.25	138.74	132.61	48.40	27.07	32.35	45.62	123.00
5-endo-acetyl	42.47	137.62	131.02	45.64	52.11	27.19	49.74	208.68, 28.98
5-endo-carbomethoxy	42.45	137.66	132.29	45.56	43.09	29.18	49.54	175.15, 51.39
5-endo-amino	42.52	140.41	131.21	48.69	50.99	46.14	35.49	
5-endo-hydroxy	42.86	140.41	130.79	48.04	72.46	37.76	48.20	
5-endo-methyl	41.56	137.29	132.09	49.41	28.70	42.10	43.48	25.52
5-endo-methoxy	42.16	138.06	131.20	47.28	81.67	44.99	34.03	56.70
5- endo-acetoxy	42.16	138.47	131.49	45.69	75.06	47.60	34.49	21.10, 171.30
5-endo-carboxyl	42.49	137.86	132.40	45.64	43.24	29.04	49.66	181.36
norbornenone	39.93	143.17	130.24	55.73	215.63	50.80	37.13	

Table 2. ^{13}C NMR SCS values (ppm) for C2 and C3 of 5-X-substituted 2-norbornenes



X	σ_I	SCS(C2) exo	SCS(C3) exo	SCS(C2) endo	SCS(C3) endo
H	0	0	0	0	0
Me				2.01	-3.19
NH_2	0.19	2.78	-0.29	5.09	-4.08
OH	0.29	4.91	-1.99	5.13	-4.49
OCH_3	0.26	5.31	-2.18	2.78	-4.08
OAc	0.33	5.61	-2.82	3.06	-3.89
C_6H_5	0.17	2.05	1.99		
Cl	0.43	5.03	-2.03		
Br	0.44	4.52	-2.01		
I	0.43	2.75	-1.85		
CO_2H	0.32	2.84	0.41	2.53	-2.93
CO_2Me	0.26	2.76	0.44	2.38	-2.99
Ac	0.31	2.95	0.50	2.34	-4.26
CN	0.56	2.78	-1.32	3.46	-2.67

Inspection of the data shows that qualitatively, the predicted pattern of shifts is obtained in most cases. However in the *exo* series, the three substituents containing the carbonyl function all have downfield shifts for C3 instead of the expected upfield ones. The phenyl substituent also exhibits an anomalous C3 shift, an even greater upfield one than that found for the carbonyl containing derivatives. In contrast, the shifts for C2 lie in the expected downfield direction for all compounds. In the *endo* series all the shifts were in the direction expected, even though, of the two, this was the series where anomalous behaviour would

most likely have been expected. The above observations are merely qualitative However from a quantitative point of view; the picture is much less satisfactory.

The simplest possible model is one assuming only the polar effect of the substituent influences shifts, with transmission of this from the substituent to the reaction site occurring by a combination of the inductive and field mechanisms. This would predict that, for both the *exo* and *endo* series, the magnitudes of the SCS for both C2 and C3 should be linearly related to the magnitude of the polar effect of the substituent. As noted in the introduction to this section, Adcock[21] observed this type of behaviour in a limited study of the ^{13}C NMR spectra of a range of 1-X-4-vinyl[2.2.2]bicyclooctanes. Graphs based on his data are shown in Figures **23** and **24**. [Note: The ρ_I values listed in these and in Figures **25-34** are based on the best line being constrained to pass through H. This is because, unlike the other points, these shifts are not subject to substituent-dependent non-electronic contributions to the NMR chemical shifts of unknown origin.]

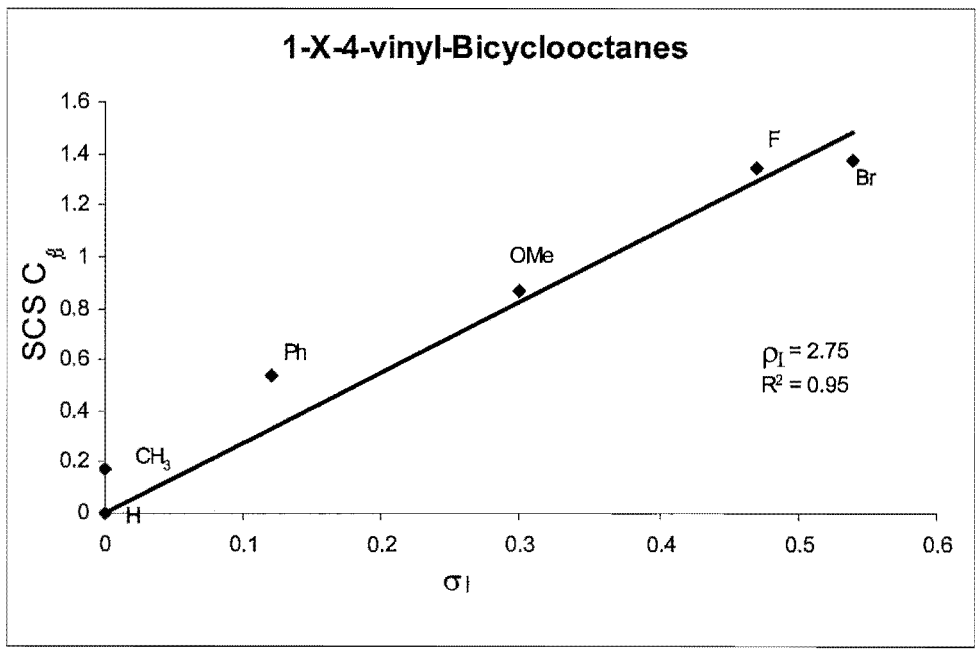


Figure 23. Plot of SCS C_β against σ_I for 1-X-4-vinyl[2.2.2]bicyclooctanes. (data from Adcock[21])

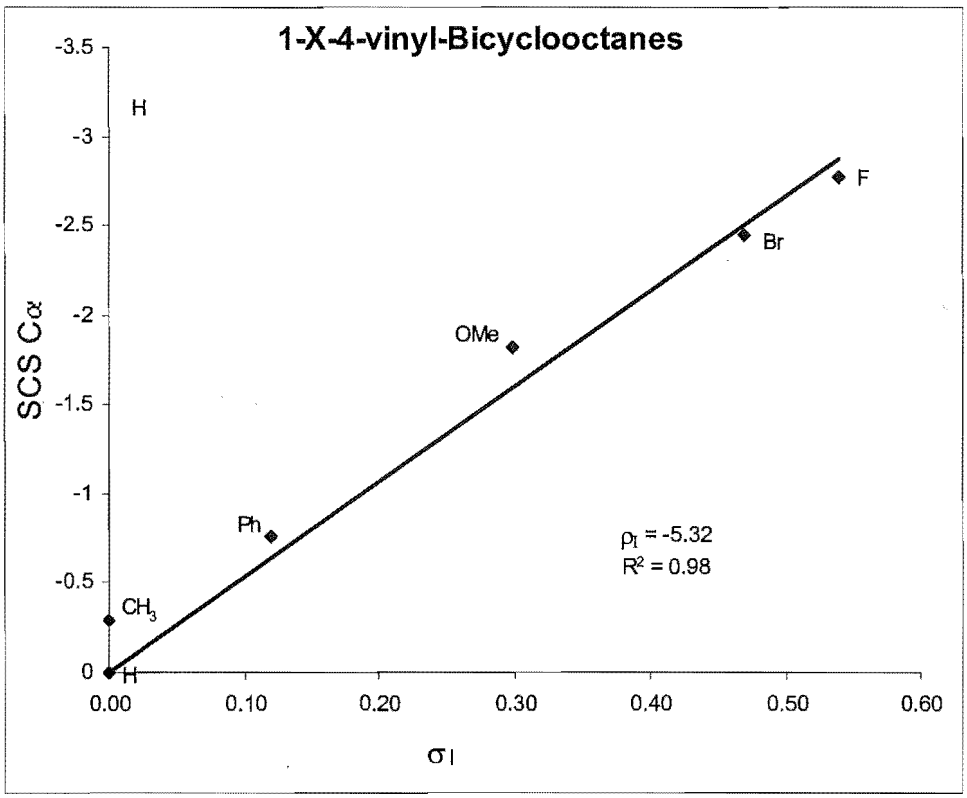


Figure 24. Plot of SCS C_α against σ_I for 1-X-4-vinyl[2.2.2]bicyclooctanes. (data from Adcock[21])

Unfortunately the range of substituents he used was very limited, and of these, only H, OMe, Br, and Ph were also used in my study. However he did obtain data covering a wider range of substituents with alternative groups in the 4-position as probes (-CH=CCl_2, -CH=CF_2, -C≡CH, and $-C_6H_5$). Those that gave the best correlations with σ_I were the last two of these. Both gave very good ones for both the carbon nearest to the bicyclooctane ring (C_α or C_{ipso}) and the more distant one (C_β or C_{para}) with σ_I. Plots of these shifts against σ_I follow (Figures **25, 26, 27 and 28**).

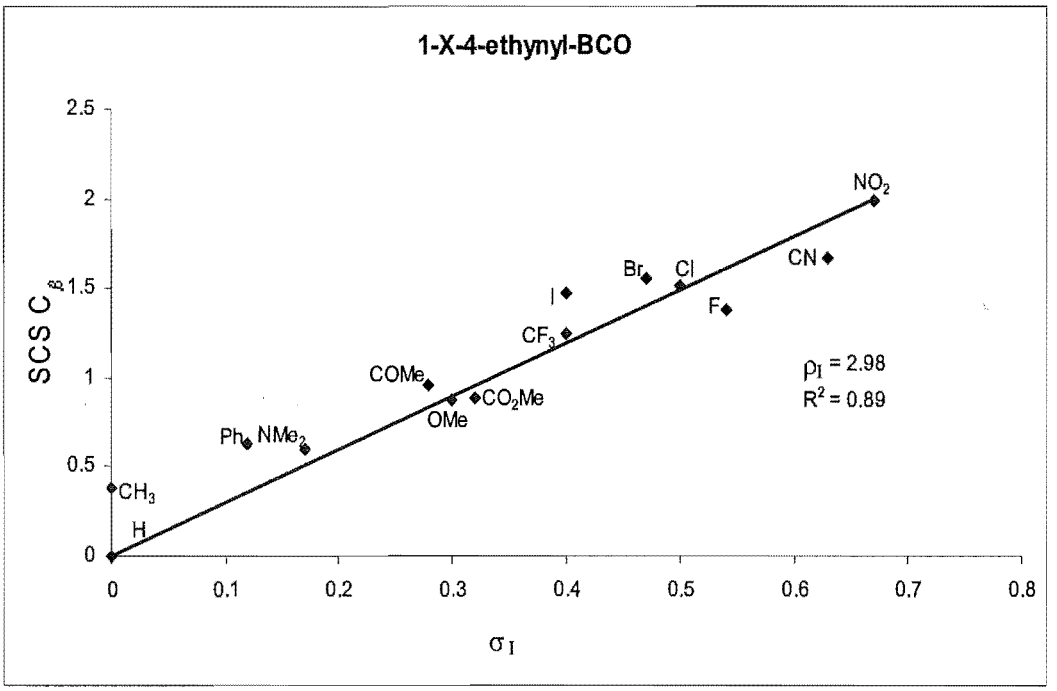


Figure 25. Plot of SCS C_β against σ_I for 1-X-4-ethynyl[2.2.2]bicyclooctanes. (data from Adcock[21])

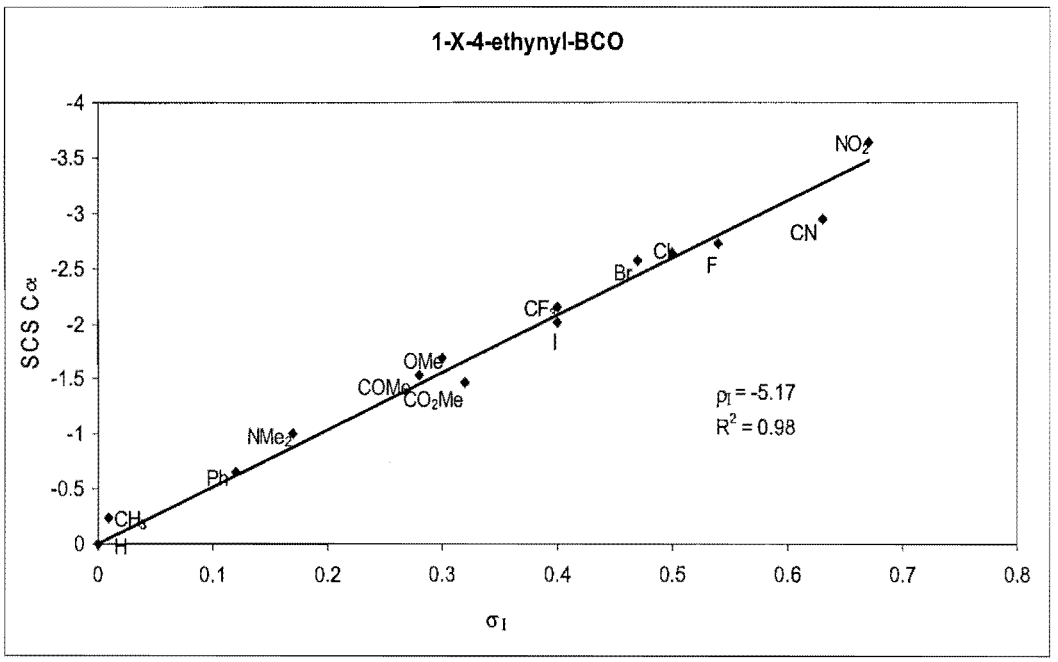


Figure 26. Plot of SCS C_α against σ_I for 1-X-4-ethynyl[2.2.2]bicyclooctanes. (data from Adcock[21])

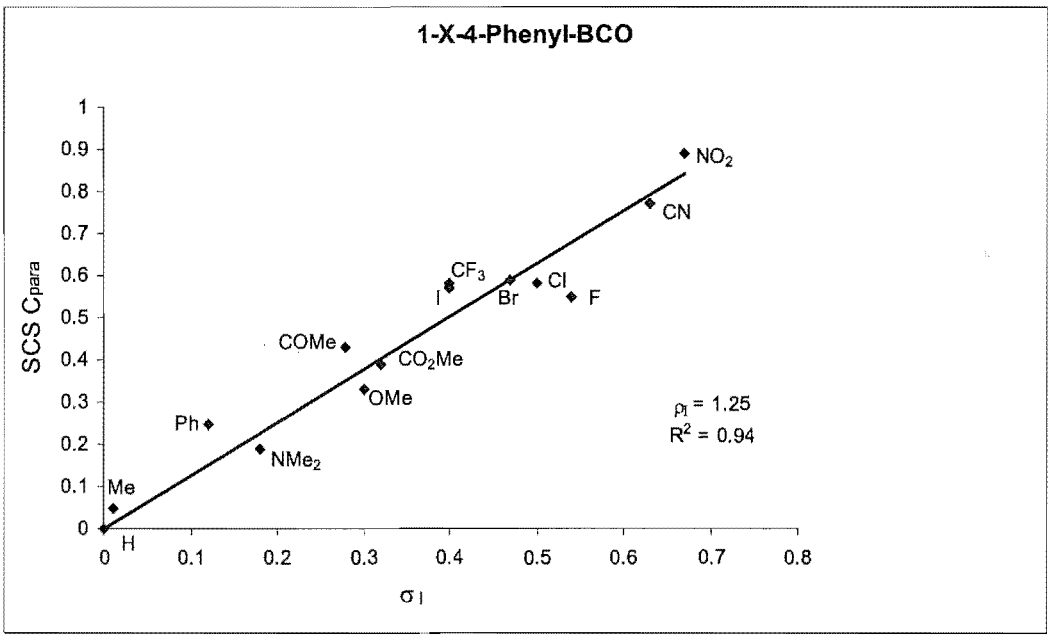


Figure 27. Plot of SCS C_{para} against σ_I for 1-X-4-phenyl-[2.2.2]bicyclooctanes. (data from Adcock[21])

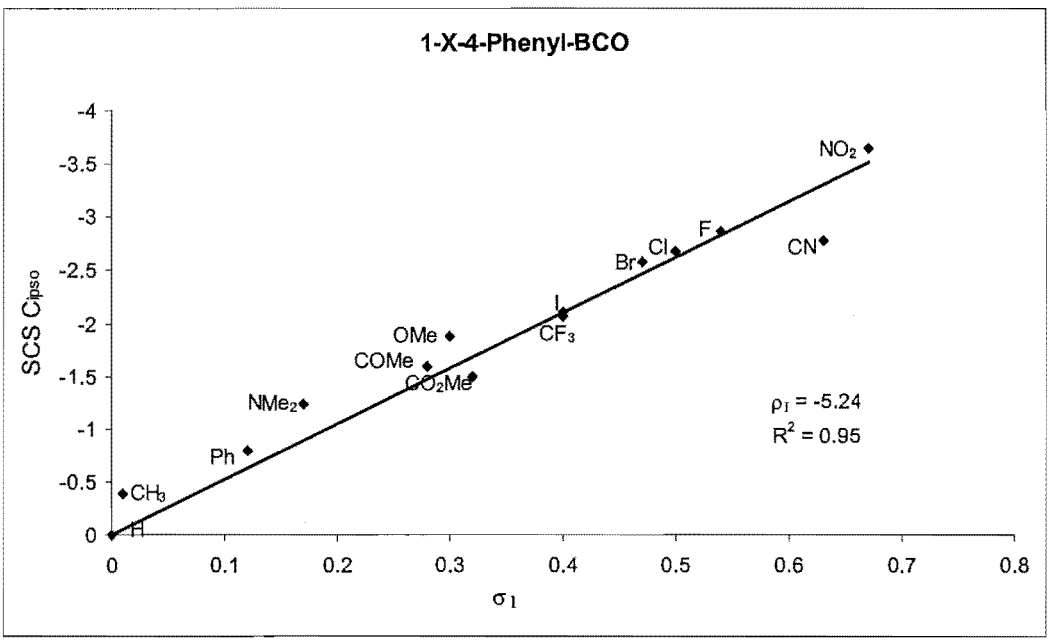


Figure 28. Plot of SCS C_{ipso} against σ_I for 1-X-4-phenyl[2.2.2]bicyclooctanes. (data from Adcock[21])

In all three of these systems, there exists an approximately linear relationship between the SCS(X) of C3 and C2. They are consistent with the polar effect of a substituent X being the major factor influencing the shifts of both the nearer and more distant carbons of a π system linked to C4 in the 1-X-4-[2.2.2]bicyclooctanes. The result is also consistent with the main role of the intervening skeleton being one of attenuating this effect either via a through-bond inductive or a through-space field effect. It is what one would expect if the the polar affect of X simply distorted the π system, without allowing any 'leakage' of π electrons from the probe site into the bicyclooctyl cage.

It is interesting to consider the slopes of the lines, which represent the ρ_I values for the systems. For all three they are very similar for the shifts of the carbon of the probe that is the nearer to the substituent. The ρ_I values for carbons bonded to C4 that form part of other π systems also studied by Adcock (-CH=CCl_2, -CH=CF_2, -CN, -CH=O, -CO_2Et) turn out to be similar in magnitude and sign (see Table 3).

Table 3. Summary of ρ_I values for 1-X-4-Y substituted [2.2.2]bicyclooctanes[21]

Y	-CH=CH_2*	-C≡CH	-$C_{6\,H5}$	-CH=CCl_2	-CH=CF_2	-CN	-CH=O	-CO_2Et
ρ_I (C_α)	-5.32	-5.17	-5.24	-5.44	-4.04	-3.66	-4.54	-3.64
ρ_I (C_β)	+2.75	+2.98	+1.25**	+3.45	+0.00			

*The corresponding values for the α and β side-chain carbons of styrenes, where the distance between the substituent and the probe is virtually the same as in the 1-X-4-vinyl-[2.2.2]bicycloctanes, are -2.7 and +4.11 respectively.[40]

**C_{para}

Inspection of this data above shows that there is a slight relationship between ρ_I for these carbons and the electron-attracting ability of the other component of the π system, with low ρ_I values being associated with systems in which the more distant end is strongly electron attracting. This is not unexpected, as the more tightly the π electrons are retained at this end, the more difficult it is for a -I substituent to attract π electrons to the other end of the bond, and

consequently induce an upfield chemical shift. This interpretation is consistent with the ρ_I values obtained for the more distant carbons of the first four probes. The very low ρ_I value for the β carbon of the β,β-difluorovinyl series implies that the highly electronegative fluorines make it very difficult for the substituent to influence the electron density on this carbon. In such circumstances it is perhaps surprising that the effect of substituents on the chemical shifts of the α carbon is as great as it is.

The norbornene skeleton is quite similar to the [2.2.2]bicyclooctyl one from the point of view of dimensions. Examination of models shows that the carbons of the six-membered ring present in both, if projected on to a flat surface, lie remarkably close to those of a benzene ring. The C2 and C3 carbons of norbornene are virtually the same distance from a substituent at C5 as the C4 and C3 ones in monosubstituted benzene are from the substituent. In addition, a substituent occupying an *exo* position does not deviate much from the mean plane of the six-membered ring. The same is not true, however, of the 5-*endo*-norbornenes, where the substituent is essentially at right angles to the plane of the ring. Since my study is concerned with the polar effect of substituents, and the polar effect is considered to operate mainly via a through-space field effect, this means that the probe of the polar effect (here a C=C bond) may experience very different fields when the substituent is *endo* to that when it is *exo*. For this reason it is advisable to discuss the two series separately. This will be done, and I will start by considering the *exo* series, since this is the one for which the widest range of substituents was available, and which, structurally, bore the closest resemblance to the [2.2.2]bicyclooctane and benzene systems.

2.9(i) Interpretation of the Chemical shift data for C2 and C3 of the 5-X-exo-2-Norbornenes

While the 5-X-*exo* norbornene system may to some extent be regarded as a variant of Adcock's 1-X-4-vinyl[2.2.2]bicyclooctane one, the differences between the two are in fact quite considerable. Chief among these differences are:

1) The C=C bond is not free to rotate, as it is in the 4-vinyl [2.2.2]bicyclooctanes. (Note, however, that in the 4-ethynyl and 4-phenyl series, even though free rotation is possible, such rotation should make no difference to the orientation of the probe). Offsetting this advantage is that in norbornene the C=C bond cannot be treated as independent of the core molecular skeleton.

2) The C-X substituent dipole is significantly closer to both ends of the norbornene C=C bond (and especially so to C3). As a result, both the inductive through-bond effect and the field effect would be more strongly experienced by the π bond than in the [2.2.2]bicyclooctane series.

3) The more distant alkenic carbon (C2) lies closer to X, in relative terms, than the more distant one on the vinyl group of a 1-X-4-vinyl-[2.2.2]bicyclooctane. As a result, an electron withdrawing X attracting electrons away from C2 towards C3 by polarising the C2-C3 π system, would be at the same time partly offsetting this via the inductive effect involving C5→C6→C1→ C2.

4) The polar effect represents primarily a field effect, and the magnitude (and even direction) of this will depend on the relative orientations in space of the C-X bond and the probe. This means that the magnitude of the polar effect of X experienced by the probe could vary according to whether X occupies an *exo* or an *endo* site, and that both of these should differ from that in a 1,4-[2.2.2]bicyclooctane system, where the alignment is essentially parallel.

5) The main potential difference, and also the most complicated to interpret, is that mentioned previously — the possibility of the existence of some form of interaction between bonding orbitals on the π system and ones on C5. Any such interaction would immediately invalidate any assumption that the norbornyl skeleton is acting merely as a 'spacer'.

Bearing the above factors in mind, let us consider the correlations that result when the shifts of the two alkene carbons in the 5-*exo*-2-norbornene series are plotted

against σ_I. Graphs of the SCSs for C2 and C3 against the σ_I values used by Adcock are presented below in Figures **29** and **30***.

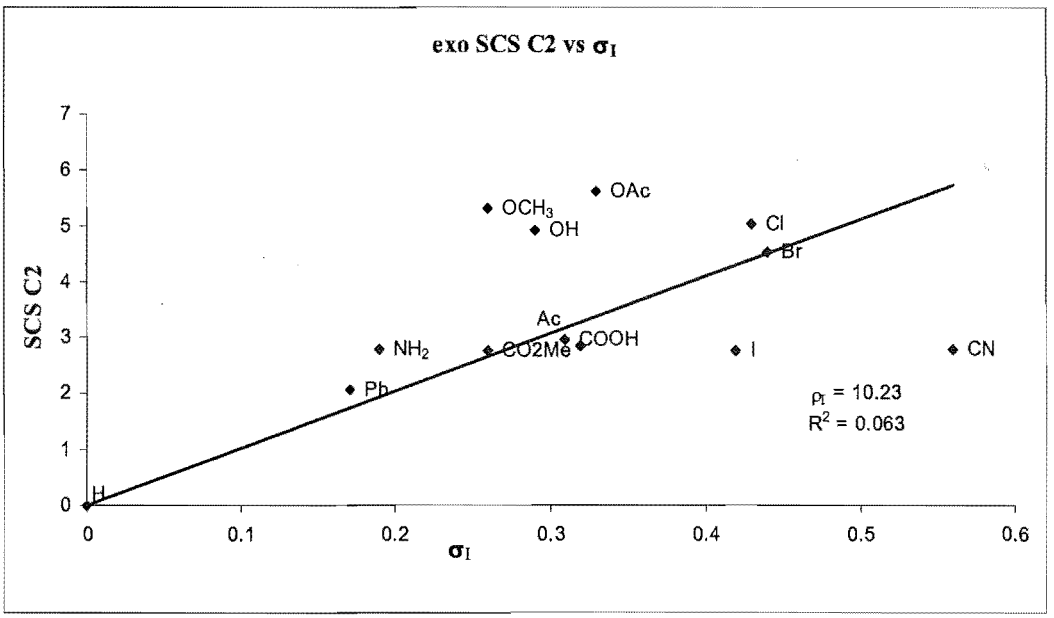


Figure 29. Plot of SCS C2 against σ_I for 5-*exo*-X-substituted-2-norbornenes

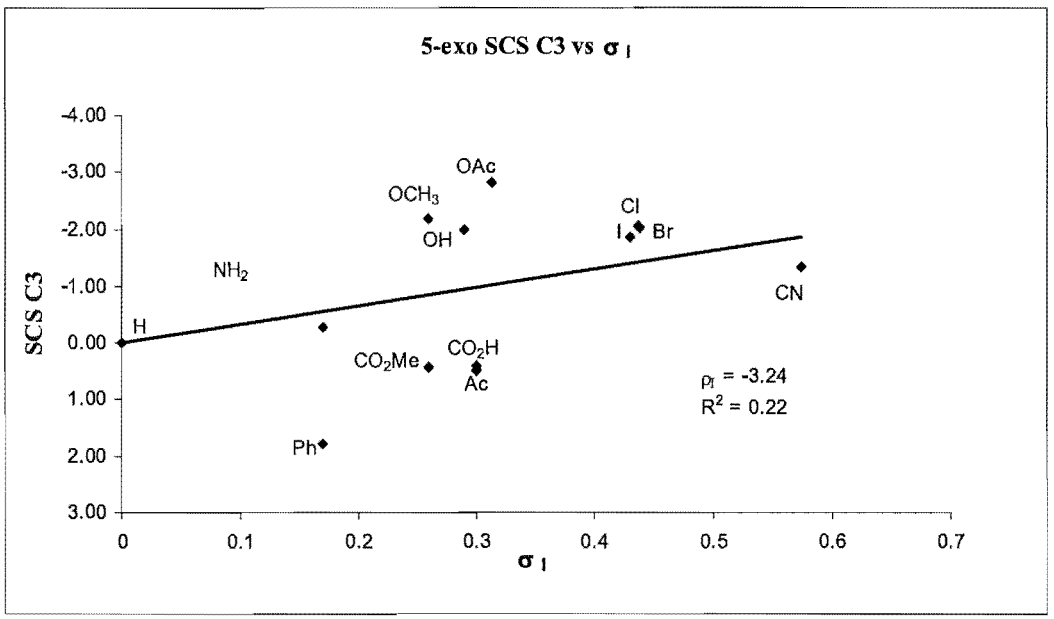


Figure 30. Plot of SCS C3 against σ_I for 5-*exo*-X-substituted-2-norbornenes

* Note that the regression lines have been constrained to pass through H. This is because, unlike theother points, these values are not subject to substituent-dependent non-electronic contributions to the NMR chemical shifts of unknown origin.

The most obvious conclusion that can be drawn is that the correlation is poor for C2 and even worse for C3. Examination of the graph for C2 shows that some degree of correlation with polar effects is probably involved, in that electron withdrawing substituents induce downfield shifts in the SCS for these carbons, but clearly the relationship far from quantitative. Some substituents (e.g. OMe/OH/OAc) appear to be polarising the π bond much more than expected on the basis of their polar effect, while others (I, CN) much less. It should be borne in mind, however, that this is relative, since the above comments are based on the (arbitrary) assumption that the shifts for Ph. NH_2, CO_2Me, Ac, CO_2H, Cl and Br are approximately 'normal'. However it could be that, for example, it is the ones for OMe/OH/OAc that are 'normal' and that it is the others that are behaving abnormally. There is evidence for the clustering together of some substituents of closely related types such as OMe/OH/OAc, CO_2Me/CO_2H/Ac, and Br/Cl but no obvious explanation for the apparently anomalous behaviour of I (relative to Br/Cl) or CN, both of which induce downfield shifts that are only about half that anticipated on the basis of their σ_I values. The slopes of the best lines through the points (constrained to pass through H) are about +9.59 for C2 and -3.12 for C3, but these are virtually meaningless, given the scatter in the points.

The C2 and C3 carbons lie two bonds closer in the norbornene system than the corresponding ones in the bicyclooctyl one. It is commonly accepted that a typical fall off factor for polar effects is about 2 for each additional bond, so that on this basis, one would have anticipated ρ_I values of about +10 to +12 for C2 and -20 to -25 for C3. For C2, the discrepancy is not great, although the fit is poor, but for C3 the figure obtained (-3.12) is very much lower than would have been anticipated. Accounting for the observed shifts, therefore requires not only explaining the relatively poor correlations observed, but also the much lower than expected sensitivity of the C3 chemical shifts to polar effects.

In seeking an explanation for the anomalous behaviour, one should bear in mind that, since the polar effect of a substituent would be expected to affect the chemical shift at C2 or C3 by an amount that is proportional to its magnitude, a poor correlation with σ_I may simply mean that this trend is being obscured by

factors that are either absent in molecules such as the 1-X-4-[2.2.2]bicyclooctanes, or, if they are present, are small relative to the polar effect. There are many substituent properties that do not affect chemical reactions, but that can influence ^{13}C NMR chemical shifts significantly, so that a poor correlation may merely serve to indicate that one or more of these is contributing substantially. The extent of such contributions is likely to more sensitive to distance than polar effects, and operate through bonds rather than through space, so the lesser number of bonds separating the substituent and probe could well lead to non-electronic effects that are small enough to be ignored in the [2.2.2]bicyclooctane system being much more significant in the norbornyl one. There is some evidence that supports this in that the data for C3 correlate much more poorly with σ_I than those for C2. Unfortunately little is known about these factors, which means that while the data may reflect them, it cannot identify them, and they cannot be allowed for. The best one can hope to do is to assume that factors such as these are not major contributors to the shifts, and seek explanations that offer reasonable alternatives.

There are clear signs that the norbornyl framework is interacting in some way with the π system. Most notable of these is the unexpectedly low sensitivity of the chemical shifts for C3 to the polar effect of the substituents. The relevant ρ_I values are summarised below in Table 4, together with ones for styrenes and α-*t*-butylstyrenes derived from data available in the literature.

Table 4. ρ_I values* for alkenic carbons of norbornenes, bicyclooctanes,[21] styrenes[40] and α-*t*-butyl styrenes[42].

	-CH=CH-(NB)	-CH=CH_2 (BCO)	styrenes	α-*t*-Bu- styrenes
C_α or C3	-3.12	-5.32	-2.7	-2.43
C_β or C2	+9.58	+2.75	+4.11	+1.88

*slopes of best lines passing through H.

The factors involved can be seen by considering the ρ_I values listed in the table for the bicyclooctanes, styrenes and α-*t*-butylstyrenes. If the response to substituent effects in the 4-vinyl-[2.2.2]bicyclooctane series is regarded as

'normal' as far as polar effects is concerned, then in the styrenes, where the distances and spacial relationships between the substituent and side-chains is virtually the same, the transmission of polar effects from the terminal (β) carbon is about 50% more efficient than 'normal' while that from C_α is only about 50% of 'normal'. This is the consequence of an additional mechanism of transmission of polar effects coming into play. Since π bonding electrons are more polarisable than σ ones, the π ones in the aromatic system will be distorted more readily than the σ ones in the bicyclooctane skeleton, with the result that the total 'inductive' contribution to the polar effect will be enhanced. The presence of the aromatic π system in the styrenes, and, in particular, its ability to overlap with that of the vinyl group, has a further consequence — ρ_I for C_α is substantially smaller in magnitude than ρ_I for C_β whereas in the bicyclooctanes it is higher, as would be expected for a carbon closer to the substituent This lower than expected ρ_I for C_α in styrenes implies that the distortion of the electron density on the vinyl group arising from the operation of the field effect leads to a much smaller build up in electron density on C_α of a styrene than on the corresponding α carbon in the bicyclooctane series. The most obvious explanation for this is that there is overlap of the π systems of the aromatic ring and the vinyl side chain and that the missing electron density is being passed on to the π system of the whole system. Let us next consider the α-*t*-butylstyrene system, where overlap of the two π systems is restricted by the presence of the bulky *t*- butyl group. Polarisation by the substituent of the π systems of both the aromatic nucleus and the side-chain can still occur, but since overlap of the two is prevented, polarisation of the π system as a whole no longer occurs. The effect of this is to make substituent-induced decreases in electron density on the terminal (β) carbon of the side chain less than in the styrenes (they are approximately halved). However the loss of coplanarity of the two systems means that the mechanism by which the buildup of charge on C_α is dissipated over the π system of the ring can no longer operate, so the side-chain is polarised independently of the rest of the system. This interpretation accounts satisfactorily for the differences in the ρ_I values for C_α and C_β in the two styrene series. However it does not explain why the sensitivity to polar effects in the α-*t*-butylstyrenes is significantly lower than in the

bicyclooctanes. These are the same distance from the substituent as the vinylic carbons in the bicyclooctane series, but appear to be less sensitive to polar effects. It is difficult to envisage a mechanism by which the relay of substituent effect is lower, although it is possible that the electronic effect of the *t*-butyl substituent may play a role.

If we now apply the principles discussed to the 2-norbornenyl system, we must first bear in mind that the ρ_I values listed in Table 4 are not very reliable and can be regarded as no better than an indication of their true ones. The carbons of the C=C bond in the norbornenes lie two carbons closer to the substituent X. On this basis a figure of around +10 for ρ_I of C2 would not seem out of line. On the other hand one of around -3 for C3 is clearly far lower than expected for a carbon separated from the substituent by only two carbons, rather than the four carbons intervening in the corresponding bicyclooctane one. It is very clear that there is very little substituent-induced build up of electron density on C3. The only possible explanation is that it is being dissipated into the norbornyl skeleton by some means. In other words, the bicycloheptane system is able to act as an electron acceptor.

The data are to some extent consistent with the effect of substituents on the ^{13}C NMR chemical shifts of monosubstituted benzenes. Taft and co-workers[15] have measured the ^{13}C NMR chemical shifts of a range of these and analysed the shifts of the *para* ring carbons using his DSP (dual substituent parameter) equation. For this carbon he found that the data in $CDCl_3$ solvent gave a good correlation with σ_R^0, with $\rho_I = 4.54$ and $\rho_R = 21.54$. This carbon bears the same relationship to the substituent X as the C2 one in a 5-X-substituted-2-norbornene. The C3 one in the latter corresponds to a *meta* ring carbon of a monosubstituted benzene. One would expect that a *meta* ring carbon would be insensitive to resonance effects, but respond to polar effects, but although the first is true, the second is not — it is widely recognised that ^{13}C NMR shifts of *meta* carbons in monosubstituted benzenes are relatively insensitive to the substituent present and do not correlate well with its electronic effect. Values of SCS_{meta} for the

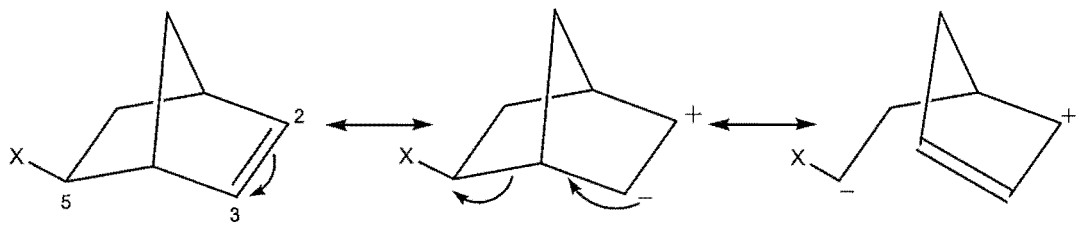
substituents included in my study taken from a compilation in the literature[43] are given below in Table 5.

Table 5. ^{13}C NMR chemical shifts of *meta* carbons in monosubstituted benzenes

X	NH_2	OH	OMe	OAc	Cl	Br	I	CO_2H	CO_2Me	Ac	CN	Ph
SCS	+0.8	+1.35	+1.04	+0.4	+1.4	+1.6	+1.6	-0.1	-0.1	-0.1	-1.1	0.4

It will be noted that while there does seem to be a variation with substituent, this is small and there is no indication that polar effects are contributing to this. It is possible therefore that the same factors are responsible in both cases.

If any build up of electron density on C3 due to polarisation of the π bond is eased by their delocalisation into the norbornyl skeleton, then by what mechanism can this be achieved? It would apparently require that a saturated skeleton act as a π acceptor. One possibility is that it is relayed from C3 to the skeleton by electron delocalisation (see resonance forms (**31**) below):



(A)

(31)

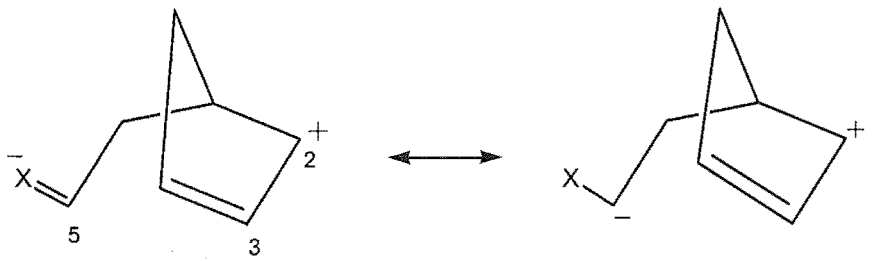
For such a pathway to play a significant role, (**A**) must make a sufficient contribution to the structure of the molecule to induce a change in the chemical shift at C3. While the contribution of such a form to the overall structure is likely to be very small, very little positive charge needs to be present on C2 in order to induce a substantial change in its chemical shift. (The cationic carbon of the isopropyl cation has a ^{13}C NMR chemical shift of > 300 ppm whereas the observed shifts in our NMR study are of the order of 5 ppm or less.) If X is a –I group (as all of those studied were) the contribution of (**A**) would be enhanced by its ability to stabilise negative charge on C5. Such enhancement should be

roughly proportional to the σ_I value of X, and so might be expected to pass unnoticed. However, if X were also capable of withdrawing electrons by a resonance mechanism, this could affect the contribution of (**A**) to the structure quite considerably, and to an extent that depended on its σ_R^- rather than its σ_I.

What would we expect if delocalisation of the type proposed took place? It should lead to C4 developing some sp^2 character, and this would affect its chemical shift. Typically the ^{13}C chemical shifts of alkenes bearing an alkyl group on each of the alkenic carbons have shifts around 130ppm (that for 2-norbornene is 135.28 ppm.) The shift for the bridgehead carbons in 2-norbornene is 41.73 ppm. All of our 5-X-2-norbornenes have higher shifts than this — most are 5-10 ppm higher (See Table 1, page 35). This could be taken as support for an increase in sp^2 character for C4.

In the styrenes, as previously noted (page 47), ρ_I for the β carbon is enhanced, perhaps by 50%, relative to that in the analogous [2.2.2]bicyclooctane system. However this is not large, given the differences in the structures of the two systems. Much more significant is the difference between the two in ρ_I for the α carbons of the two vinyl groups where the change is about threefold. The probable reason for this is that overlap between the two π systems in the styrene leads to dispersal of any negative charge built up on its α carbon over the aromatic system. That coplanarity in the styrene system is involved in this dispersal is confirmed by the observation that the Cβ shifts for *para* –M substituents give good correlations with σ^- [39]. In the norbornene system the geometry is locked, with the π system of the double bond lying in approximately the same plane as the C-X bond of an *exo* substituent. This orientation should resemble that found in the styrenes more than that in the bicyclooctanes. If dispersal of negative charge generated on C3 is occurring, then, since the chemical shift may be regarded as a measure of its electron density, ρ_I for C2 be lower that what would have been expected in the absence of this. However as pointed out on the previous page, there is a further consequence if X is a -M

substituent — additional stabilisation of resonance form (**A**) by overlap with of the electrons on C5 with the π system of X becomes possible.



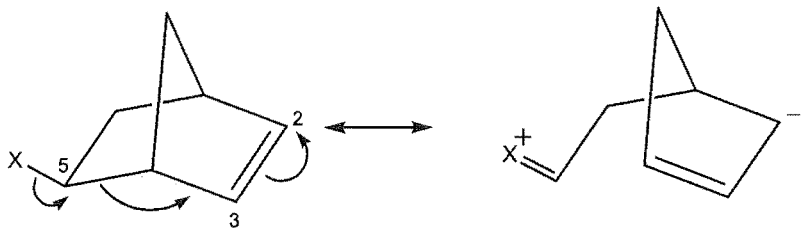
(B) **(A)**

(32)

If X is a +M substituent, forms such as (**B**) cannot occur. As a result, one might expect that with respect to the chemical shifts for C3, -I +M substituents on C5 might yield a linear correlation with σ_I, although with a lower than normal value for ρ_I because of the generally lower than expected electron density on this carbon resulting from resonance form (**A**). However –I -M ones, by removing more electron density from C3 via resonance form (**B**) than predicted from their σ_I would cause a greater than expected downfield shift in the ^{13}C NMR resonance for this carbon. Since the normal -I effect for such a substituent would be to induce an upfield shift, the two effects would be opposed. Examination of a graph of the C2 shifts against σ_I (page 44) shows that this in fact is what is observed. The (–I, +M) substituents (NH_2, OH, OMe, OAc, Cl, Br, I) while not giving a particularly good correlation, at least give one with a negative slope (-5.12). In contrast, the (–I, -M) ones lead to either slightly downfield shifts (CO_2H, CO_2Me, Ac) or slightly upfield (CN). Since CO_2H, CO_2Me and Ac are much weaker –I groups than CN, such behaviour is not unexpected. (The phenyl substituent appears to give an anomalous result. The reason for this is unknown.)

The preceding explanation is based on the assumption that -M substituents on C5 are able to help stabilise a negative charge on C3, whereas +M ones cannot. However in the styrenes it was found that both *para* –M and *para* +M substituents interacted by a resonance mechanism with the vinyl group, and that the latter could affect the chemical shift of the terminal (β) carbon. Therefore it is possible that direct resonance interaction between a substituent on C5 and C2 is possible.

How this can occur can best be illustrated by considering the possible resonance forms. For –M substituents, the key one involved is (**B**) on the previous page. For a +M one, an additional one (**C**) is involved:



(**C**)

A contribution from (**B**) should lead to an abnormal downfield shift in C2, while one from (**C**) would lead to an abnormal upfield one in the same carbon. However examination of the data in Table 1 (page 35) and Figure 29 (page 44) show that +M substituents seem to have caused downfield shifts. (The position with regard to –M ones is unclear, but they certainly do not appear to have caused substantial downfield ones.) The only explanation I can offer for this apparent anomaly is that when X is a +M group, resonance forms such as (**C**) do not contribute significantly to the electron density distribution at C2. This suggests that the true ρ_I value in Figure 29 is somewhat higher than that calculated (one based on +M groups only would be about 12), and it is the shifts for the –M X groups that are anomalous. There is no obvious mechanism by which the latter should induce upfield shifts at C2, so the problem must remain unresolved, a situation that is unfortunate and far from satisfactory.

Probably the most important point about the results overall is that the correlations, in contrast to those obtained by Adcock on 1-X-vinyl-[2.2.2]bicyclooctanes, were far from satisfactory. They are better interpreted as indicating trends, rather than numerical correlations, because there are clearly substituent-dependent factors contributing to the shifts other than polar effects.

2.9(ii) *Interpretation of the Chemical shift data for C2 and C3 of the 5-X-endo-2-Norbornenes*

In the 5-X-*exo*-norbornenes the C-X bond is directed away from the C=C bond, and the two lie in approximately parallel planes. These planes are sufficiently close together for the approximation that they lie in the same one is not an unreasonable one to make. However in the 5-X-*endo*-norbornenes, the relationship between the C=C and C-X bonds is very different. The planes are less parallel, further apart, and the C-X bond is constrained in such a way that it is directed not away from, but towards the double bond. (In fact examination of a model shows that the atom of the substituent directly linked to C5 lies almost directly below C3. As a result, whereas in the *exo* series the ^{13}C NMR chemical shifts of C2 and C3 could be interpreted by comparing them with ones for the corresponding 1-X-4-vinyl-[2.2.2]bicyclooctanes and monosubstituted benzenes, there is no justification for doing so in the *endo* series.

There are two major consequences of the difference in the geometries of the two isomeric series. The first is that whereas in the *exo* one the steric effect of X could be ignored because it was directed away from the double bond, in the *endo* it can become a factor. The substituent X and C3 lie close enough together for some form of proximity effect to become possible, particularly if X is large or strongly dipolar. However any interaction with C2 would be much less, because of the greater distance involved. The second consequence is that the the polar effect of X will have two components, an inductive one and a field one. The inductive (through bond) component should be independent of whether X occupies an *exo* or *endo* site. However this is normally considered to contribute considerably less to the total polar effect than the field effect generated by the C-X dipole. The strength and orientation of this field will depend on the orientation of the C-X bond, and this is very different in the two series. As a result, the overall effect of the substituent on the chemical shifts of the two alkenic carbons in the *endo* series will be the sum of three factors, the σ-inductive effect, the through-space field effect, and a possible steric effect. In addition to these,

analysis of the data will be complicated by the same possibility of delocalisation of the π system into the molecular skeleton that existed in the *exo* series. A final unfortunate complication to any interpretation is the absence of data for one important group of substituents, the halogens. The data on the compounds studied was given in Table 2 (page 36). In Table 6 below the *endo* data from this table, together with the corresponding *exo* data (where available) are given.

Table 6. ^{13}C NMR SCS values (ppm) for the C2 and C3 of some 5-X-substituted norbornenes

X	σ_I	SCS(C2) endo	SCS(C3) endo	SCS(C2) exo	SCS(C3) exo
H	**0**	0	0	0	0
Me	**0***	2.01	-3.19		
NH_2	**0.19**	5.09	-4.08	2.78	-0.29
OH	**0.29**	5.13	-4.49	4.91	-1.99
OCH_3	**0.26**	2.78	-4.08	5.31	-2.18
OAc	**0.33**	3.06	-3.89	5.61	-2.82
CO_2H	**0.32**	2.53	-2.93	2.84	0.41
CO_2Me	**0.26**	2.38	-2.99	2.76	0.44
Ac	**0.31**	2.34	-4.26	2.95	0.50
CN	**0.56**	3.46	-2.67	2.78	-1.32

*There is some uncertainty as to this value. In saturated systems it is commonly assigned a value of 0.

Inspection of the data above shows that the main difference between the two series is that in the *endo* one all of the substituents induce a substantial upfield shift in position of the resonance of C3. It was noted and discussed in the previous section that in the *exo* series there appears to be a considerable 'leakage' of electron density from this carbon into the rest of the skeleton. Any tendency for the C=C bond to be polarised independently should lead to some sort of correlation with σ_I being observed. Scatter plots of the shifts for C2 and C3 against σ_I are given on the next page.

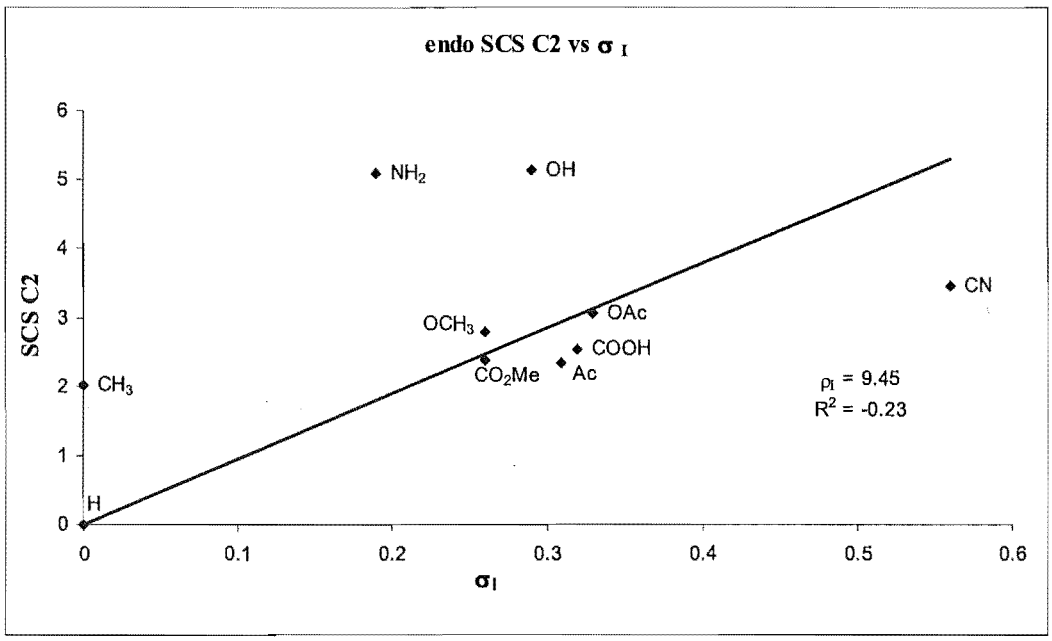


Figure 33. A plot of values of SCS for C2 against σ_I for 5-*endo* substituted-2-norbornenes*.

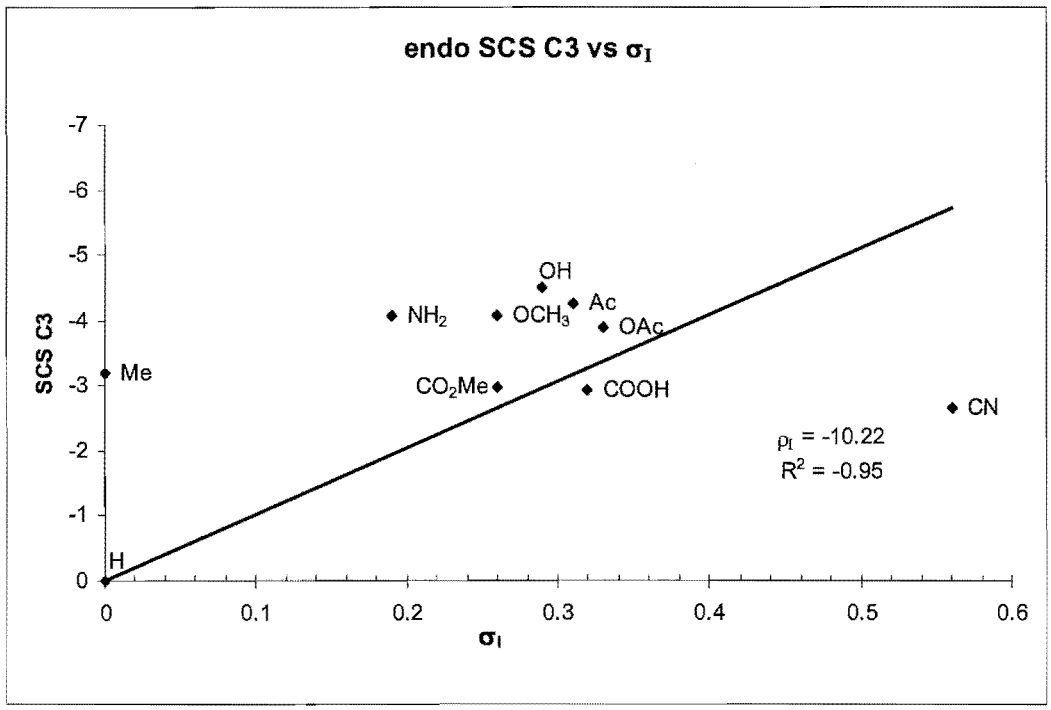


Figure 34. A plot of values of SCS for C3 against σ_I for 5-*endo* substituted-2-norbornenes*.

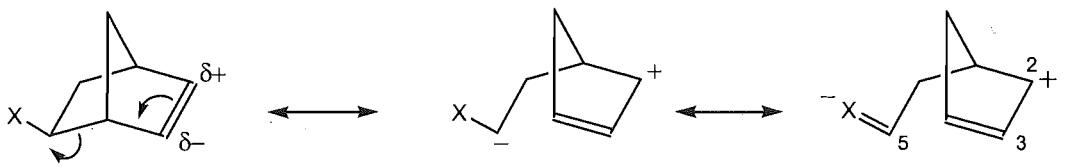
* Note that the regression lines have been constrained to pass through H. This is because, unlike the other points, these values are not subject to substituent dependent non-electronic contributions to the NMR chemical shifts of unknown origin.

The correlation with C2 would be expected to be the better, because it is the more distant from the substituent and proximity effects are less likely to be a factor. However, neither correlation is particularly good. The slopes of the best lines (constrained to pass through H) are +8.49 and -9.15 respectively. Such values, although unreliable, are not out of line with what might be anticipated (although one might have expected ρ_I for C3 to have been somewhat higher as it is closer to the substituent). In the case of C2 the figure is comparable with that in the *exo* series. However one would have had more confidence in the values had data for at least two of the halogeno substituents been available. For C2 the shifts for the $-NH_2$ and –OH groups relative to those for -OMe and -OAc would seem particularly anomalous. It is possible that the first two of these, in particular are interacting (possibly via H-bonding) with the C=C bond.

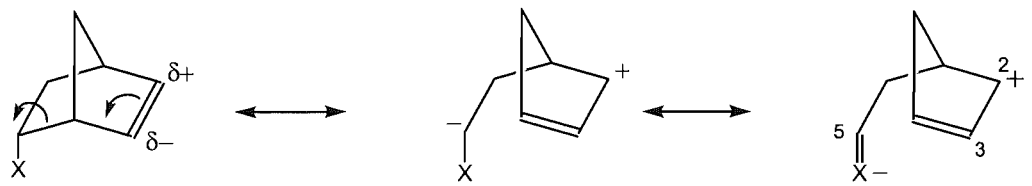
That ρ_I for C2 is similar in magnitude (although not in sign) in both series in spite of the substantially different orientations of the C-X bond in space is unexpected. The most obvious explanation, that the major contributor to the effect in both series is the through-bond inductive effect, rather than the through-space field effect, conflicts with what is generally accepted regarding the relative importances of the two. However the geometry of the system, which would constrain an *endo* C-X bond to an orientation almost at right angles to the π bond could conceivably lead to the field effect being small. If this is indeed the situation, the problem then turns to one of explaining why the ρ_I obtained for both C2 and C3 are so high relative those for the *exo* series. However the poor correlations with σ_I obtained in both series do not inspire confidence in the ρ_I values obtained, so judgement on this point should perhaps be reserved.

Nevertheless, polarisation of the C=C bond does occur in the *endo* series, and in a direction consistent with the recognised polar effect of the substituent present. In marked contrast to the *exo* series though, this apparently does lead to a build up in electron density on C3. This raises the question as to why the apparent 'leakage' of electron density from C3 in the *exo* series into the skeleton is much higher than in the *endo* one. At first sight there does not seem any obvious reason why the proposed explanation for dispersal in the *exo* case should not also apply

to the *endo* one as well. However, given that this does not appear to happen, it would seem that for some geometrical reason resonance form (**B**) apparently makes a much greater contribution to the structure in the *exo* series than (**B'**) does in the *endo* one.



(B)



(B')

Unfortunately there appears to be no obvious reason why, if X is a –M substituent, it cannot be just as important a contributor as in the *endo* series as in the *exo* one.

This type of behaviour has a lot in common with Grob's proposal of the involvement of 1,3 bridging between C2 and C6 during the solvolysis of *exo* and *endo* 6-substituted arenesulfonates. He invoked such bridging to account for differences in the effect of the *exo*- and *endo*-X isomers on the rates of solvolysis of the 2-*exo*-tosylates. He suggested that the back lobe of the C-X bond in the *exo* series interacted with the developing positive charge on C2 (C3 in our system) and assisted departure of the tosylate. In the *endo* series such an interaction was not possible because the back lobe was not directed towards C2. In our system, we have suggested that the excess of π electrons on C3 of the norbornene are being stabilised by the incipient π electron deficiency on C5, and that this is only geometrically possible when X is *exo*. The differences between the two are that (a) in my system it is proposed that it is the π electrons on X that are involved, whereas he considers it to be the back lobe of the C-X σ bond, and (b) in his

system the interaction occurs to assist stabilising a positive charge at the reaction site, while in ours it assists in stabilising a developing negative charge.

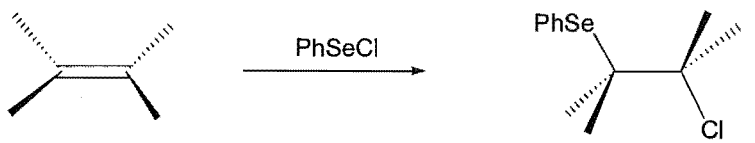
Basically,although there are many unanswered questions in this work the results are consistent with the π electrons of the C=C bond in a 5-X- substituted norbornene in some circumstances interacting with a π system on X, provided X is a π acceptor and is in the *exo* and not the *endo* position. Such an interaction could well be too weak to be detectable by techniques other than ^{13}C NMR, although in favourable circumstances careful determination of the structures of suitable compounds by X-ray diffraction might pick up small variations in the bond lengths involved. However, as I subsequently found out (see Chapter 4)), disorder problems in crystals of compounds of this type mean that the determination of accurate bond lengths is extremely difficult.

Chapter 3

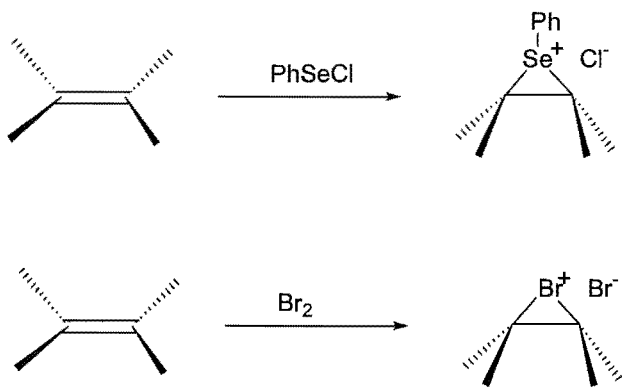
THE REACTIONS OF PHENYLSELENYL CHLORIDE WITH 2-NORBORNENES

3.1 Introduction

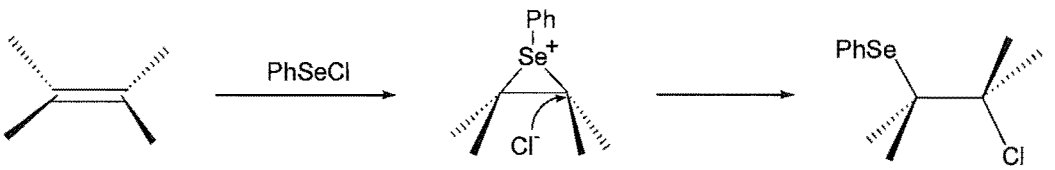
Phenylselenyl chloride reacts readily with alkenes to form β-chloroselenides:[44,45]



The reaction is stereospecific and gives products in which the PhSe and Cl add to opposite sides of the double bond. In this it resembles the addition of bromine[46] to alkenes, and the reasons for the stereospecificity are the same in both cases. It arises as a result of the electrophilic portion of the reagent (a phenylselanyl group or a bromine) adding to the alkene to form a cationic species in which the phenylselanyl or bromine is bonded to both carbons simultaneously. (That both do this is not really surprising, as selenium and bromine are similar in size, occupy adjacent positions in the periodic table, and the electronic structures around the selenium in $PhSe^+$ and bromine in Br^+ are essentially the same.)

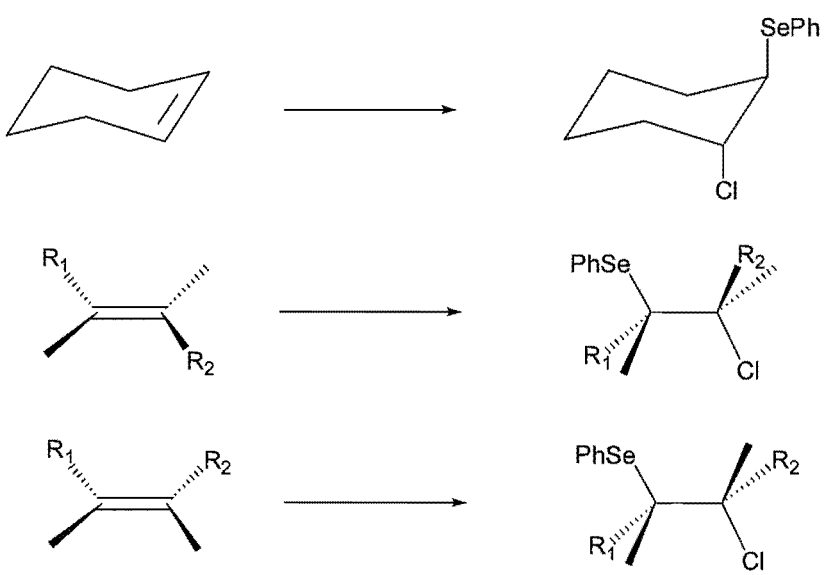


The three membered ring formed during the phenylselenyl chloride addition (a seleniranium ion)[47] should carry most of the positive charge present on its selenium. Adducts containing such rings are moderately stable and can even be isolated[48,49] if the counterion is a relatively non-nucleophilic one such as SbF_6^- or PF_6^-. However in the course of PhSeCl additions to alkenes it is cleaved in a second step as a result of bimolecular nucleophilic attack on one of the carbons by the chloride counterion. This second step presumably occurs by an S_N2 pathway, and requires approach by the latter from the opposite side of the carbon to the selenium[50](**35**).



(35)

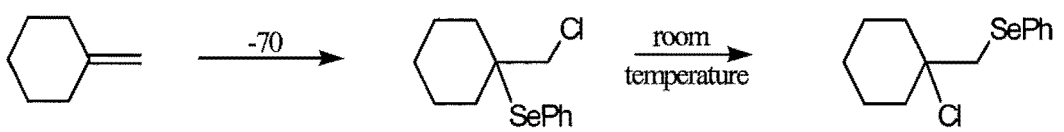
Supporting this pathway is the observation that cyclic alkenes invariably give *trans* products, (*E*)-alkenes *erythro* ones, and (*Z*)-alkenes *threo* ones.



The basic reaction has been the subject of a considerable number of kinetic studies[45,51-54]. As a result of these Schmid and Garratt[55] proposed a general reaction scheme for the reaction of an (*E*)- alkene of the type RCH=CHR' that in

their view accounted for the observations. It was a rather complex one, and involved the initial formation of two selenirane intermediates in which the chlorine was directly bonded to the selenium. These subsequently ionised to give five distinct ion-pairs that in turn yielded the two possible isomeric products.

Addition of PhSeCl to unsymmetrical alkenes[56] introduces the possibility of regioisomer formation, and as with the addition of most unsymmetrical electrophilic reagents[57,58] to unsymmetrical alkenes, usually both isomers are formed. Since the first step is an electrophilic addition, one would expect Markovnikov's rule to be obeyed, and this is normally what happens for addition of phenylselenyl chloride to simple alkenes at room temperature. The formation of Markovnikov products normally indicates that the reaction is under thermodynamic control. However there have been a number of reports of anti-Markovnikov additions occurring under some conditions. In particular, at low temperatures, the kinetic product, in which the chloride ion attacks the least hindered carbon is favoured. The addition of phenylselenyl chloride to methylenecyclohexane in dichloromethane at -70° is one example. Ho and Kolt[59] reported that at this temperature 1-chloromethyl-1-phenylselanylcyclohexane (**36**) is the sole product. However on warming this to room temperature the product mixture rapidly isomerises to the more thermodynamically stable 1-chloro-1-phenylselanylmethylcyclohexane, (**37**):



(**36**) (**37**)

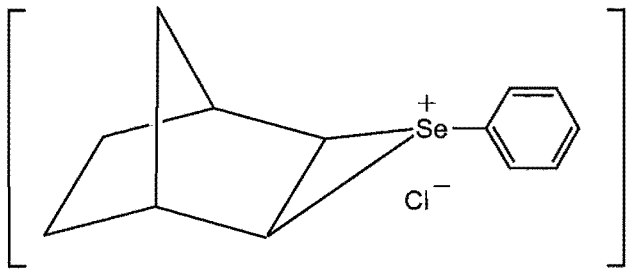
This particular example is a rather extreme one — the tertiary carbon of the seleniranium ion intermediate is highly hindered to S_N2 attack. Consequently the chloride ion much prefers to open the ring by reacting at the unhindered primary carbon to yield the anti-Markovnikov product. This is the reaction that occurs at -70°. However at higher temperatures the reaction presumably can reverse to re-form the bridged seleniranium ion, as a result of S_N2 attack by the selenium on the relatively unhindered primary carbon. Re-formation of the

seleniranium ion gives the chloride ion further opportunities to add to the tertiary carbon and form the Markovnikov product. However reversal of Markovnikov product formation by S_N2 selenium attack will be discouraged because the tertiary carbon is highly hindered. Although chloride ion could be lost by an S_N1 mechanism, such unassisted ionisation would lead initially to an unbridged cation. Such a species can only reconvert to the antimarkovnikov product via the bridged ion, and the relative stability of the unbridged tertiary cation would not encourage this. It is interesting to note that this behaviour leads to the opposite temperature dependence to that observed for addition of hydrogen halide or halogen to 1,3-butadiene, where higher temperatures favour the halogen ending up on the less substituted carbon.

There have been a number of studies of the effect of alkene structure on the ratios of the products formed. At room temperature markovnikov products are normally favoured, except for 1,2-disubstituted alkenes, which can give both isomers (unless one of the groups is an aryl group, or else much larger than the other). At low temperatures antimarkovnikov products are often formed, except for additions to trisubstituted alkenes[60-64].

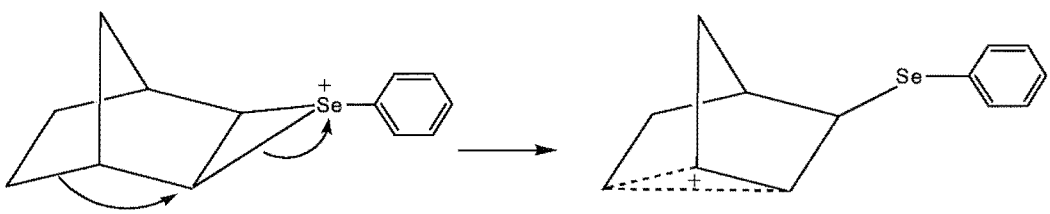
3.2 Addition of phenylselenyl chloride to norbornenes

The situation with respect to norbornene[65] is interesting if viewed along the above lines. For steric reasons the phenylseleneny halide would undoubtedly favour attack at the *exo* face. The two carbons C2 and C3 are identical, and, as previously noted, most of the positive charge on the seleniranium ion (**1**) would probably be carried by the selenium. The polar effect of a cationic[66] selenium would make C2 and C3 sufficiently electron deficient to encourage bimolecular attack on these by nucleophiles such as the chloride ion(**38**). Regardless of which of the two carbons is attacked, the same product would be formed.



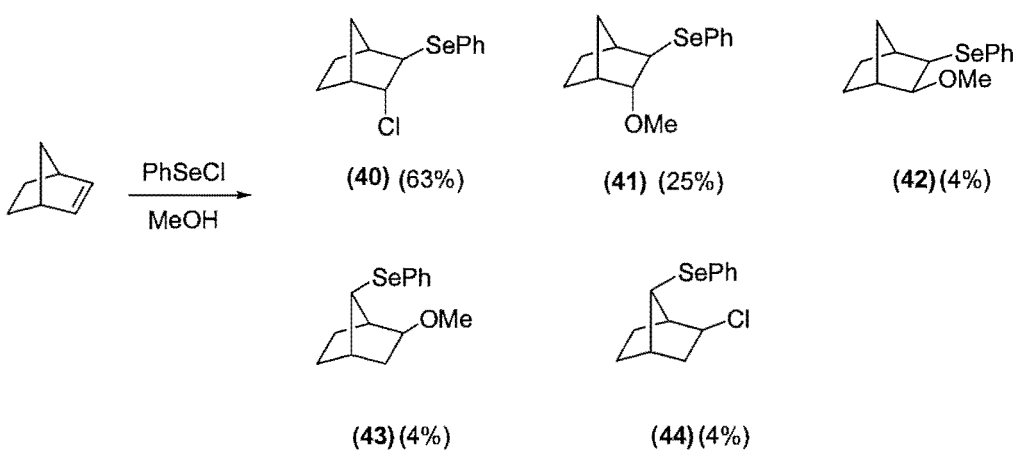
(38)

However if the inductive effect is sufficiently great, the electron deficiency at C2 (or C3) might be great enough for stabilisation by the C1—C6 (or C2—C5) bond to develop. The result of this could be that, instead of an *exo*-bridged seleniranium ion one might be dealing with the non-bridged non-classical 3-phenyselanyl-2-norbornylcation (**39**). Unlike the bridged ion, this species is not symmetrical.



(39)

Garratt and Kabo[67,68] studied the reaction of phenylselenyl chloride with a number of alkenes in dichloromethane and in methanol. Among them was norbornene. They observed that in methanol five products were formed.

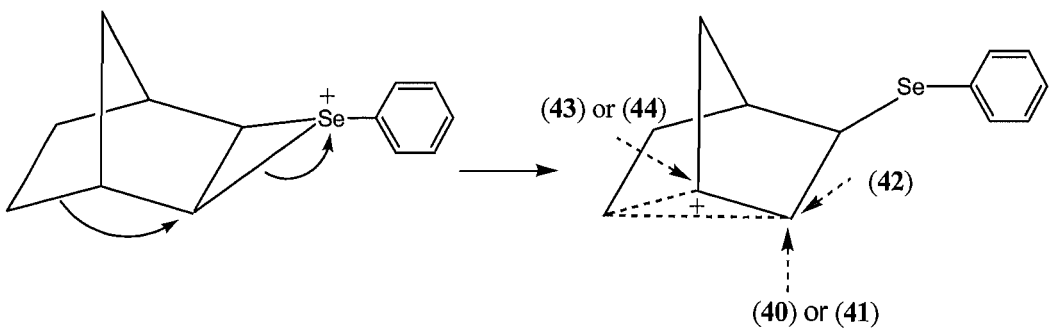


(40) (63%) **(41)** (25%) **(42)** (4%)

(43) (4%) **(44)** (4%)

The formation of (**41**), (**42**), and (**43**) shows that at some point in the reaction methanol competes with chloride ion as a nucleophile. This is not unexpected. The formation of (**43**) and (**44**) implies the involvement of a non-classical cation at some point. The formation of (**40**) as the major product even in methanol is not a surprise, and is consistent with initial reaction of the phenylselenyl chloride with norbornene to give the ion-pair (**38**). It is reasonable to expect that at least some (**40**) would form as a result of bimolecular attack on C2 or C3 by the chloride ion even in methanol solvent, because the charge on the chloride encourages it to remain in the proximity of the cation. The other product formed in significant amounts is (**41**), and its formation indicates that the ion-pair is sufficiently long-lived under the conditions for the solvent to compete with chloride ion in opening the ring. That the methoxy group, like chloro, prefers to take up an *endo* position suggests that the formation of both (**40**) and (**41**) arises as a result of S_N2 attack by chloride ion or methanol on an *exo* seleniranium cation rather than their adding to an unbridged cation.

The problem lies in accounting for the formation of products (**42**), (**43**) and (**44**). These are ones expected to be formed if the bridged seleniranium cation, in which the positive charge is essentially entirely on the selenium, opens to give the linear non-classical 3-phenylselanyl-2-norbornyl cation (**39**). Reaction of (**39**) with either methanol or chloride ion could give rise to any of (**40**) – (**44**).



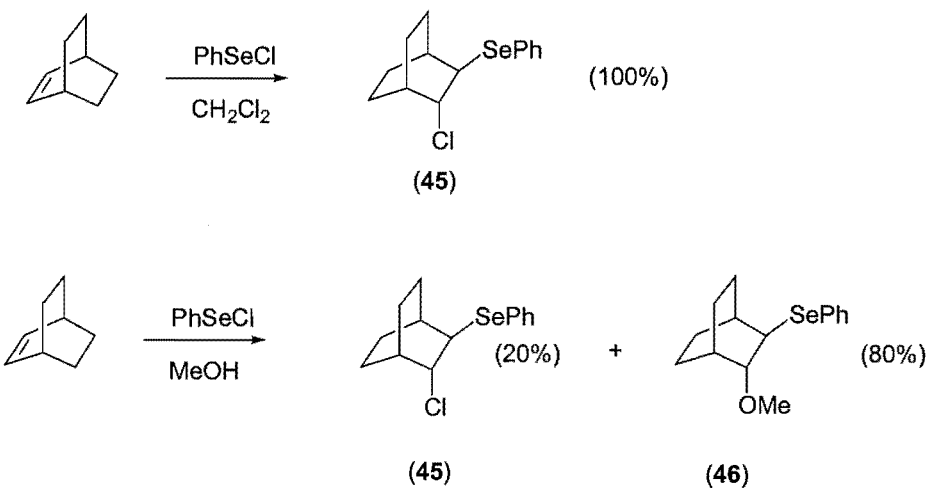
(**39**)

The relative product yields would suggest that in methanol solvent about 80% of the total product is formed as a result of S_N2 attack on the seleniranium

ion and 20% via the non-classical cation. (Some (**40**) and (**41**) could arise from addition of methanol or chloride ion to C2 of (**39**).) There is no obvious explanation for the absence of the chloro analogue of (**42**). In support of this interpretation it has been reported[49] that addition of selenenyl halides to arylpropenes in which the aryl group bears strong electron donating substituents leads to adduct formation that is less stereospecific than expected[69-72]. This was attributed to the bridged seleniranium cation in these reactions being less stable than the open carbocation.

When Garratt and Kabo carried out the same reaction in dichloromethane instead of methanol, the sole reaction product was (**40**). The absence of (**44**) as a product implies that the nonclassical seleniranium cation (**39**) is either not formed in this solvent, or if it is, is present in very low concentration. The major point of difference between the two systems is that dichloromethane is much less polar than methanol, and as a result is less capable of stabilising ions. Such conditions encourage attack by the chloride ion on the seleniranium cation, and, by shortening the lifetime of the ion pair, this allows less opportunity for skeletal rearrangement of the bridged ion to (**39**) to take place.

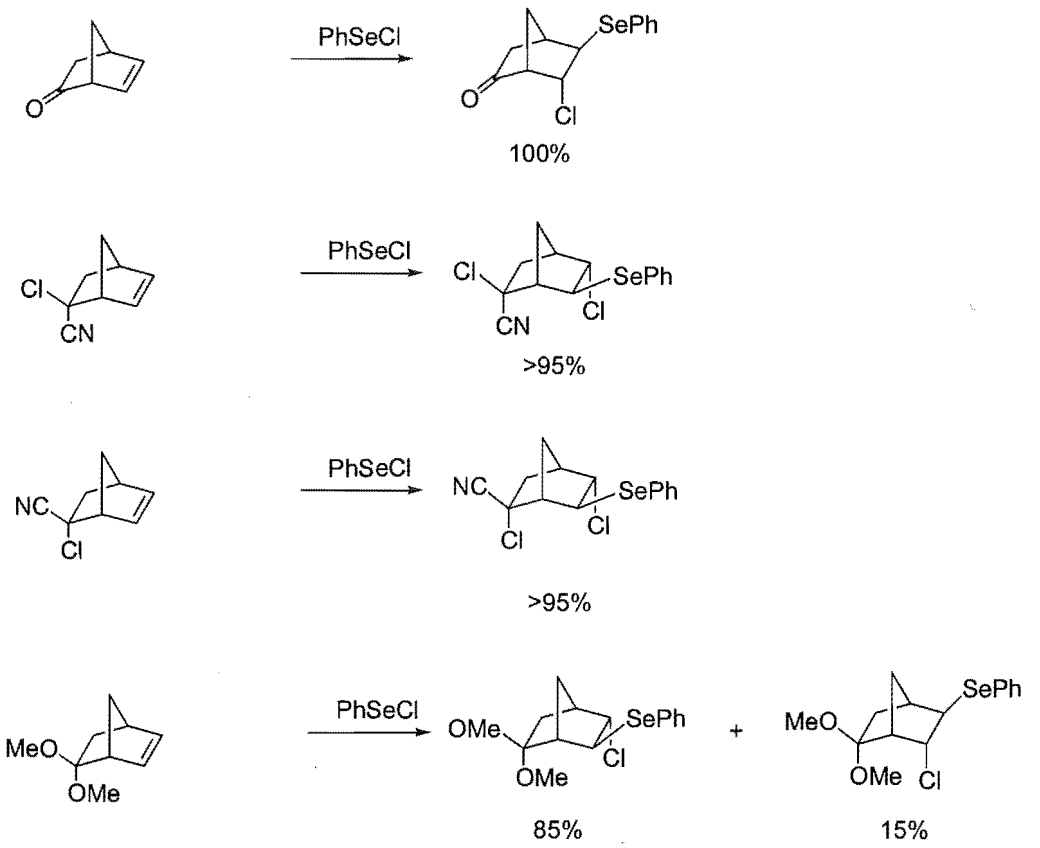
Garratt and Kabo also reported results for the corresponding reactions of [2.2.2.]bicyclooctene[67]. In dichloromethane, as with norbornene, only the normal *anti* adduct (**45**) was formed. However, in methanol (**45**) was the minor product, the major one being (**46**), the analogous methyl ether.



A comparison of the relative yields of methyl ether and chloride with those obtained with norbornene in methanol shows that methanol is more effective as a competitor than chloride ion in [2.2.2]bicyclooctene by a factor of around 10. This is a little unexpected, since the geometrical environments *anti* to the C—Se bond in the two intermediates should not be all that different. It may be that the cation is less strained and has a longer lifetime. .More importantly, though, there were no products found in which the phenyselanyl and chloro/methoxy groups were not on adjacent carbons, which argues against any involvement of a nonclassical ion as a reaction intermediate. It should be borne in mind, though, that even if a nonclassical species were present, compounds analogous to (**42**), (**43**), and (**44**) might have been formed, but if the yields were very low, their presence may not have been observed.

3.3 Addition to 5-substituted norbornenes

There have been no previous investigations of the effect of a single substituent occupying either a C5 *exo* or *endo* position on the orientation of addition of phenylselenyl halides to the C2—C3 double bond of norbornene. However Carrupt and Vogel[73,74] studied additions of arylselenyl halides to 2-norbornenone, the two 5-chloro-5-cyanonorbornenes, and 5,5-dimethoxynorbornene. For the reaction of phenylselenenyl chloride in chloroform they obtained only the 6-*endo*-chloro-5-*exo*-phenylselanyl-2-norbornanone from the ketone, but mostly the other regioisomer for the others (see below).

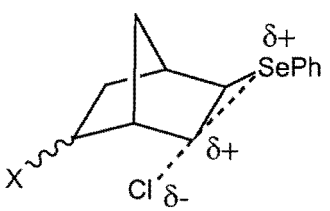


In the last three reactions the substituents on C5 are all electron attracting, and the regiochemistries of the product(s) obtained are mainly those arising from a strong preference for attack by chloride ion taking place *endo* to the C2 carbon. The authors rationalised the result in terms of it being consistent with any buildup of positive charge on the C3 carbon being discouraged as a result of the presence of electron attracting substituents on C5. (This discounts the possibility that *endo* attack at C3 is disfavoured on steric grounds — an *endo* substituent on C5 could well make attack at C3 more difficult.) In contrast, for 2-norbornenone, attack at C6 is heavily favoured. Steric effects would be unimportant in this instance. Here electronic factors are more likely involved. Unfortunately the polar effect of the carbonyl group should discourage attack at this site. To explain the apparent anomaly Carrupt and Vogel[74] proposed that such discouragement was more than offset by stabilisation gained as a result of hyperconjugation involving the C5-C6 bond, enhanced by the presence of the C=O group. In other words, the homoconjugated carbonyl group was behaving as an electron donor rather than an electron withdrawer.

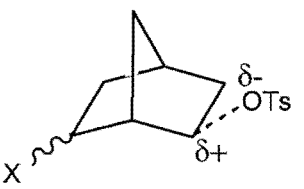
There have been a number of other studies of the regiochemistry of additions to norbornenes and/or related substrates[75]. Arjona and co-workers have studied the addition of phenylselenyl chloride and bromide to some 5-substituted-2-norbornenes[76] and the same reagents, together with phenylsulfenyl chloride, and phenylsulfenyl bromide to 5-substituted 7-oxabicyclo[2.2.1]heptenes[77-79]. More recently, Tam and co-workers[80,81] have investigated the regiochemistry of the oxymercuration of 5-substituted *exo* and *endo* norbornenes. However the value of both studies was diminished by the relatively limited range of substituents used.

During the 1970s and early 1980s Grob and co-workers[82] carried out a series of studies on the rates of solvolysis of a number of 6-substituted-2-norbornyl arenesulfonates, with the aim of examining the influence of the polar effect of the substituent on the rate. Among the series he studied were the 6-X-*exo*- and 6-X-*endo*-2-norbornyl *exo* and *endo* tosylates[83].

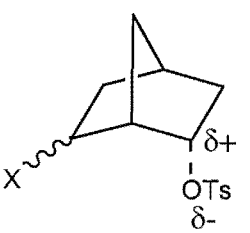
The solvolyses were carried out under conditions that favoured an S_N1 mechanism. The effect of a substituent on reaction rates for an S_N1 reaction may be regarded as a measure of its ability to stabilise the charge on the transition state for that reaction. The transition state for attack by chloride ion at C2 in the second step of phenylselenyl chloride addition to a 5-substituted 2-norbornene would involve a transition state (**47**) that has a lot in common with the transition states[84] (**48**), (**49**) in Grob's solvolyses[85,86]



(47)

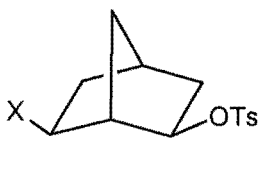


(48)



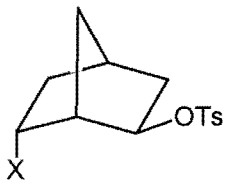
(49)

Consequently the rate of attack at C3 by chloride ion could well respond to substituent effects in a similar way. Grob found that there was a good relationship between his rate constants and σ_I in all cases.



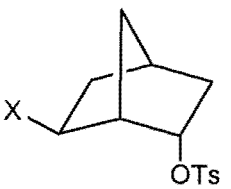
(50)

$\rho = -2.0$



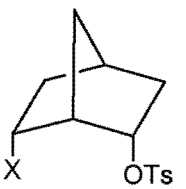
(51)

$\rho = -1.75$



(52)

$\rho = -0.78$



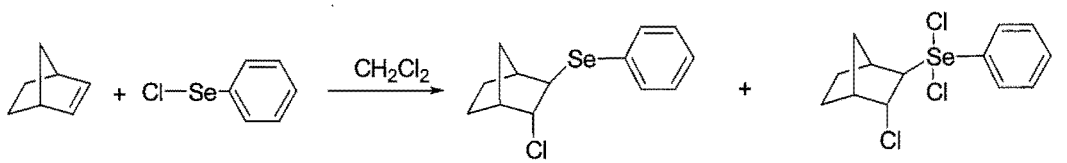
(53)

$\rho = -0.94$

Note that in all four series ρ was negative, indicating that the development of positive charge on C2 is discouraged if X is electron withdrawing. Grob attributed the high magnitudes of ρ to C6-C2 bridging, in which the back lobe of the C-X bond interacted with the developing vacant orbital on C2. However he had some difficulty in accounting for the considerable differences in the observed ρ values for (**50**) and (**52**), and also the relatively small ones for (**50**) and (**51**). The relevance of Grob's work to the present investigation will be discussed further in the *Results and Discussion* section that follows. It should be pointed out, however, that this only concerns the formation of the products arising from addition of chloride to C2. Attack at C3 should be much less sensitive to the electronic effect of X, and even less to whether it is *exo* or *endo*.

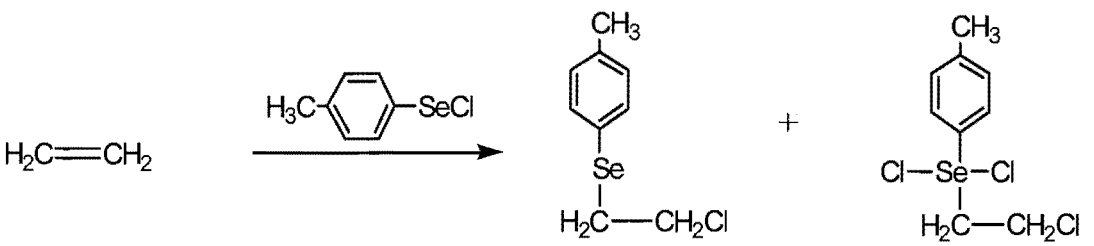
3.2 RESULTS AND DISCUSSION

In order to establish the appropriate conditions for carrying out the reaction and analysing the products, the reaction of phenylselenyl chloride with norbornene was investigated in the first instance. As noted in the introduction to this section, this reaction had been previously studied by Garratt and Kabo[67] who found that, in dichloromethane only the expected adduct (**40**) was formed. My investigation of the reaction in dichloromethane showed that not one, but two products were formed when equimolar quantities of norbornene and phenylselenyl chloride were reacted together at room temperature. One of these was the expected 2-*endo*-chloro-3-*exo*-phenylselanylnorbornane (**40**). The other, forming about 20% of the total product, was the related compound 2-*endo*-chloro-1-*exo*-phenyldichloroselanylnorbornane (**54**).



(**40**) (**54**)

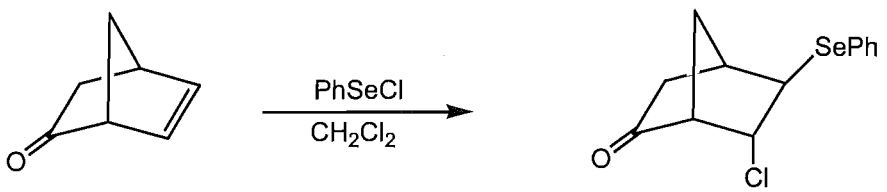
Reich and Trend[61,62] had reported a similar experience when they investigated the reaction between *p*-tolylselenenyl chloride and ethylene. Their nvestigations revealed that during the addition process, initially formed adduct was reacting further with a second molecule of *p*-tolylselenenyl chloride to form 1-chloro-2-(*p*-tolyldichloroselanyl)ethane and di-*p*-tolyl diselenide.



(**55**) (**56**)

They assumed an equilibrium between the two was involved, as addition of excess ethylene led to the formation of only (**55**), except at low temperatures. In my reaction, using a threefold excess or norbornene suppressed the formation of (**54**) entirely. Warming the crude product mixture to 60° also converted the product mixture entirely to (**40**). It should be noted that since (**54**) is formed from (**40**) by the reaction of the latter with phenylselenyl chloride,[49] then in reactions involving 5-substituted norbornenes, the regiochemistry of the initial addition could be determined even if both types of product were present. Nevertheless, in working up reaction products the solvent was evaporated using a hot water bath so as to encourage conversion of the total product to the normal adducts.

As a further check on my system, I also studied the reaction of phenylselenyl chloride with 2-norbornenone. This reaction had been previously studied in chloroform and had been show to give entirely 6-*endo*-chloro-5-*exo*-phenylselenanyl-2-norbornanone[74]. Under my conditions this was also the sole product.



3.2(i) *Reactions of 5-Substituted-2- Norbornenes with Phenylselenyl chloride*

It was confirmed that, as had been reported in the literature[67,73], phenylselenyl chloride always added to the 2,3-double bond of norbornene to give a product in which the phenylselanyl and chloro substituents added from opposite sides, and that the phenylselanyl substituent in the adduct always occupied an *exo* position. There was no reason to expect that 5-substituted norbornenes would behave any differently. However because of the presence of a substituent in the 5-position, addition would be expected to give two regioisomers. The relative amounts of each formed could vary depending on (a) the nature of the 5-substituent, (b) whether the reaction was subject to kinetic or thermodynamic control, and, (c) on whether the substituent was *exo* or *endo*. Whether the product

ratio under my conditions is subject to kinetic or thermodynamic control depends on the ease of reversibility of the addition of chloride ion to the bridged ion. It was noted earlier (p 61) that in simple alkenes the product ratio was subject to kinetic control at low temperatures, and favoured the formation of the product arising from attack of chloride ion at the less hindered carbon, but that at room temperatures or above the product mixture equilibrated to give a final composition that reflected the relative stabilities of the two products. Kinetic control tended to yield mainly the antimarkovnikov product and thermodynamic control mainly the Markovnikov one. Kinetic control to give an antimarkovnikov product is primarily the result of steric effects — the chloride ion should attack the less hindered of the two carbons faster. In an *exo*-5-substituted norbornene steric effects should be absent, and both C2 and C3 are secondary carbons. Interconversion of the two isomers will involve re-formation of the bridged ion and the product ratio at equilibrium should favour the isomer forming the stronger C-Cl bond. Breaking of the C-Cl bond at either C2 or C3 will be assisted by any participation by the C1-C6 or C4-C5 bonds respectively in stabilising the transition state, and which of the two C-Cl bonds is the stronger will depend on whether the substituent at C5 increases or decreases this effect. The experimentally determined product ratio should therefore represent a measure of the relative ability of a substituent at C5 to weaken or strengthen a C3-Cl bond. (It would be reasonable to assume that any effect on a C2-Cl bond would be relatively minor.)

The situation when the C5 substituent is *endo* is less clear. On steric grounds one would expect to obtain a lesser amount of the adduct with the Cl on C3. In addition, an *endo* X may well exert a different electronic effect from an *exo* one. This is because, even if the intrinsic effect is the same in both cases, the efficiencies with which this is relayed to C3 may be orientation dependent. There are two main mechanisms by which the polar effect of X can be relayed to C2 and C3. One is by means of a through-space field effect. In many systems the lines of force very much tend to pass through the body of the molecule as it is very often the solvent is a polar one of much higher dielectric constant. Dichloromethane, the reaction solvent used, has a relatively low dielectric constant (9.08)[87]. The

molecule probably has a dielectric constant of around 2, so while the lines of force might prefer to pass through the molecular skeleton, the degree of preference may not be all that great. Regardless, however, the efficiency of transmission of the field effect will be orientation-dependent. Probably of greater importance when X is *endo*, though is that the dipole will lie in quite close proximity to C3, and its effect on this carbon may be considerably enhanced. The other mechanism of transmission of the polar effect of X is by the inductive effect. This involves transmission by successive distortion of the sigma bonds in the molecule. Here the effect of orientation would be very much smaller. It is usually accepted that the field mechanism of transmission is much more important than the pure inductive effect[88], so a significant "orientational" factor is likely to be involved in determining the magnitude of the electronic effect on the reaction.

Related to both the steric and electronic effects is the possibility that some polar 5-*endo* substituents may well interact directly with any developing positive charge on C3 as a result of their particular structure and charge distribution. The most likely ones to fall into this category would be *endo* $-CO_2H$, $-CO_2Me$, or $-COCH_3$ groups.

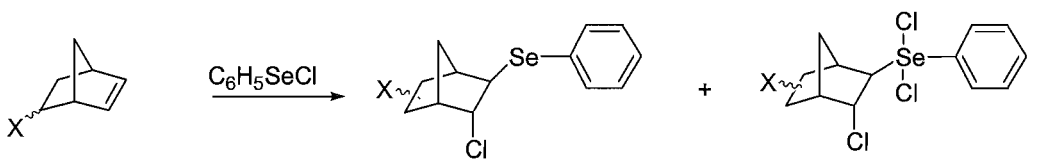
As a result of the potential problems involved in interpreting the adduct ratios obtained in additions to 5-*endo*-substituted norbornenes, and the fact that many of the alkenes can only be made with considerable difficulty, my investigation concentrated on the 5-*exo* series, which were in general easier to prepare. Some *endo* ones were investigated; the results (see later) confirmed that interpretation of the product ratios was a problem.

3.2(ii) Reactions of 5-exo-Substituted Norbornenes with Phenylselenyl chloride

A substituent occupying the 5-*exo*-position is directed away from both C3 and C2, and since both are in identical steric environments the relative yields of the two adducts obtained should be decided by electronic factors alone. The chloride ion in the first instance would be expected to show some degree of

preference for the more electrophilic of the two carbons. Since it had been found that for phenylselenyl chloride addition to methylenecyclohexane, equilibration of the two adducts took place readily at room temperature or above, it is very likely that the two regioisomeric adducts formed for addition of the same reagent to 5-X-exo-2-norbornene will also equilibrate, as from a stereochemical point of view the selenium is held in a position where attack on either of the carbons to reform the bridged ion can occur readily. Because of this, and taking into account that in my investigation reactions were carried out at room temperature, and the products heated to 60°+ during workup, the product composition measured should be that arising from thermodynamic control. However the possibility that this was not always achieved cannot be definitely ruled out.

While the products normally formed were the ones expected, rates of addition (as judged by the disappearance of the coloured phenylselenyl chloride from the solution) varied, and in cases where the addition was slow, products in which the selenium bore two additional chlorines were also formed (**57a**).



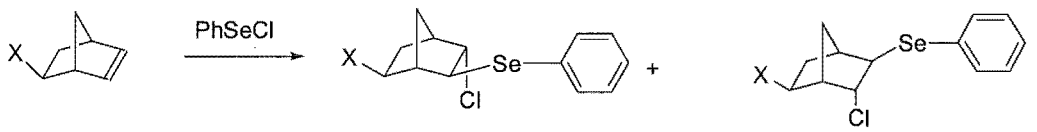
(57) **(57a)**

When this was observed formation of these was minimised by using an excess of the alkene. This confirmed that the phenyldichloroselanyl adduct was formed by reaction of the normal adduct with phenylselenyl chloride.

Problems were encountered in the addition of phenylselenyl chloride to 5-*exo*-amino-2-norbornene. Two products were formed, but only one was an adduct. The other was 5-*exo*-phenylselanylamino-2-norbornene. The relative yields of the two varied with time, with longer reaction times leading to an increased proportion of adduct being formed. This suggests that selenylation of the amino group may be reversible. There was no adduct of 5-*exo*-

phenylselanylamino-2-norbornene formed, which means that the double bond in this molecule is less reactive towards phenylselenyl chloride than 5-*exo*-amino-2-norbornene. The yields of adducts obtained for the *exo*-substituted compounds are summarised below in Table 7.

Table 7. Relative yields of adducts formed for phenylselenyl chloride addition to 5-*exo*-X- norbornenes



(57) (58)

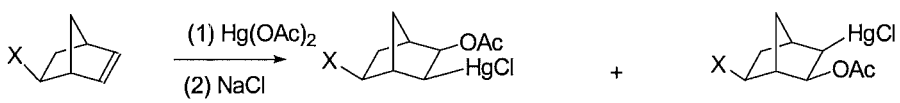
X	**%**	**%**
NH_2*	0	100
OH	10	90
OMe	29	71
H	50	50
OAc	53	47
Cl	53	47
CN	53	47
Br	56	44
I	59	41
Ac	64	36
CO_2Me	69	31
CO_2H	71	29
Ph	75	25

*The PhSeCl also reacts with the amino nitrogen of the starting material (see p. 74).

Comparisons with data obtained by other workers on related additions to 5-X-substituted norbornenes can be made, but are not particularly helpful, because the range of substituents covered by them was invariably more limited both in

number and in type. For example, Arjona and co-workers[76,79] examined the products of the reaction of 5-*exo*-X-norbornenes, but only for X = -OBn, -OH, $-CH_2OBz$, and $-CH_2OH$. With phenylselenyl bromide in chloroform or dichloromethane they found that for the first two the 2-*exo*-phenylselanyl-3-*endo*-bromide was the main product, while for the second pair the 3-*exo*-phenylselanyl-2-*endo*-bromide predominated. This can be interpreted as indicating that an electron withdrawing X in the 5-position encourages attack of the bromide ion at C3 and an electron donating one at C2. Such a trend would appear to be the opposite to that observed in my case (Table 7). The only other related investigation is that of Goddard and co-workers[81] who determined product ratios for the oxymercuration of 5-*exo*-X-norbornenes. Their range of substituents was nearly as limited as that of Arjona ($-CH_2OTBS$, $-CO_2Me$, OH, OAc, and –OTBS). Their reaction also differed from mine in that the oxymercuration reaction only gave adducts in which both substituents add *exo*. This implies a different mechanism is involved, since the second step of phenylselenyl chloride addition, bimolecular attack by the anion from the *endo* side of the molecule apparently does not occur in the oxymercuration reaction. Any conclusions drawn from comparison of their data and mine should therefore be treated with caution. Goddard's substituents were all –I ones, and the results suggested that the orientation of addition was controlled by the polar effect of the 5-substituent. Their data are summarised in Table 8.

Table 8. Product ratios for the oxymercuration of 6-*exo* substituted norbornenes



	(59)	(60)
X	**%**	**%**
H	50	50
CH_2OTBS	50	50
OH	86	14
OAc	93	7
OTBS	90	10

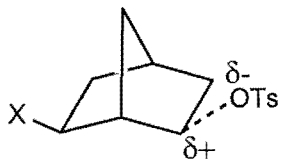
There appears to be no evidence for resonance donating (+M) substituents enhancing the formation of the Markovikov product (**60**). This could be mechanistically significant, and will be discussed further later.

In view of the shortage of data on a closely related reaction involving a suitable range of substituents, and the consequent difficulty of making reliable comparisons, the results in Table 7 will be considered in isolation. The data are listed in this in decreasing order of yield of the adduct in which the Cl is bonded to the carbon nearer to the substituent (i.e. C3). Initially it had been expected that the relative yields of the two adducts would depend primarily on the polar effect of the 5-*exo* substituent, but the observed order is not consistent with this. However all were also capable of exerting a resonance effect; with some (NH_2, OH, OMe, OAc, Cl, Br, I) being resonance donors, others (CN, Ac, CO_2Me, CO_2H) resonance withdrawers, and one (phenyl) could be either a resonance donor or resonance withdrawer, depending on the circumstances. Inspection of the data in the table shows that the presence of an electron attracting substituent in the *exo* position usually tends to encourage the formation of the 2-chloro-3-phenylselanyl adduct (**57**). However, if the substituent is both a good resonance donor, and a relatively weak polar withdrawer, formation of the 3-chloro-2-phenylselanyl adduct (**58**) is favoured.

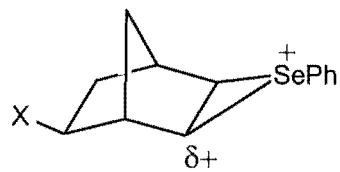
The latter observation was unexpected, especially when considered in conjunction with Grob's kinetic data for the solvolysis of 6-X-2-*exo*-norbornyl *p*-toluenesulfonates[4]. [Note: the numbering system for naming Grob's norbornyl compounds differs from that of of norbornenes — the numbering for C2 and C3 are reversed, and X is on C6 rather than C5] In this reaction, which goes by an S_N1 mechanism, a good correlation between the log k^X values and polar substituent constants was observed. As a result Grob proposed that if C2 became electron deficient during a reaction, then a bonding interaction between C6 and C2 can exist. He considered the source of electrons for such a bridging interaction to be the back lobe of the C6—X bond, and that the effect was related to the polar effect of X. In support of this, he found that when X was *endo*, in which case no such interaction was possible, the effect was absent. While he found no evidence

for a 6- *exo* X substituent exerting a significant resonance effect, the range of substituents he used was not well suited to detect this. His solvolysis rates appeared to be dominated by polar effects; and only when X was an alkyl group did they occur faster than when X = H.

Superficially, his reaction resembles mine, in that the transition state for the departure of the *p*-toluenesulfonate ion (**61**) has much in common with the structure to that of the phenylseleniranium ion (**62**):

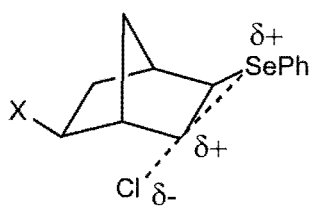


(61)

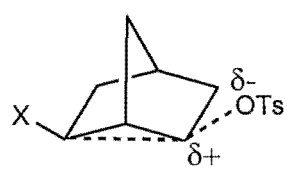


(62)

There is an important difference though. In the product-forming stage for phenylselenyl chloride addition, a chloride ion carries out an S_N2 displacement at C3 (see (**63**)). In doing so it is attacking the back lobe of the C3—Se bond, the same orbital that Grob proposed was interacting with the back lobe of the C—X bond (see (**64**)). On the basis that only one of the interactions is possible, adduct formation would only occur when a Grob-type interaction was absent. If it were present, its effect would be to discourage attack by chloride ion at C3 to give (**57**), and by default favour the formation of (**58**). The existence of competition of this form could explain why in three cases (X = NH_2, OH, and OMe) attack at C2 of the alkene is preferred to attack at C3.



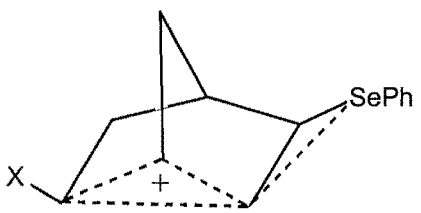
(63)



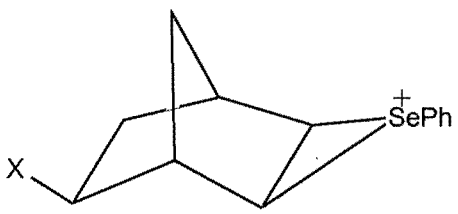
(64)

However the relative abilities of X to discourage attack in this way follow the order NH_2 >> OH >> OMe >> OAc ≈ Cl, Br, I and this also happens to be the

order of their strengths as resonance donors, so any mechanism by which a +M substituent could encourage attack at C3 could also account for the product distributions. Superficially, this would seem consistent with electronic effects in general – a resonance donor in an appropriate position should be able to stabilise an electron deficient centre on an adjacent carbon. However in this case the carbon is not adjacent, but one further away, which raises the problem of how the resonance effect of X on C5 is relayed to C3. Normally transmission involves overlap of π orbitals, so if an *exo* resonance donor stabilises a positive charge there is a strong implication that it is interacting with a suitably oriented vacant π orbital adjacent to it. In our system any electron deficiency that occurs during adduct formation would normally be at either C3 or C2. The logical mechanism by which an electron deficiency on C3 could be relieved by a resonance donor on C5 would be if it was generated there but delocalised over C3, C4, and C5. In other words, the intermediate for the formation of (**58**) when X is a strong resonance donor would have to be the nonclassical (**65**) rather than the classical bridged ion (**66**).

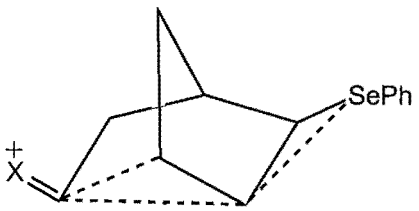


(**65**)



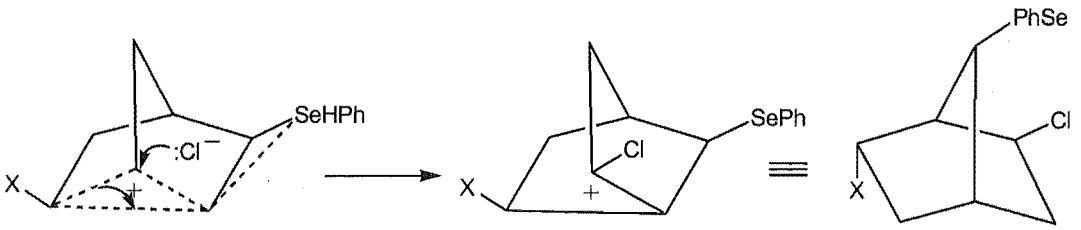
(**66**)

The stabilisation arising when X is a resonance donor would presumably be that due to contributions from the resonance form (**67**).



(**67**)

Unfortunately, if the intermediate for the formation of adduct (**58**) is (**65**), then one might expect to find among the products the adduct (**68**), formed as a result of attack of chloride ion at the bridgehead carbon, C4. These were not found.



(**68**)

However bimolecular attack by Cl^- at C4 would be hindered by steric hindrance from either X or the phenylseleniranium ring, depending on which side attack occurred from, and the stereochemistry of the transition state involved would also be unfavourable. Additions of bromine to alkenes, like phenylselenyl chloride additions, also involves bridged cationic intermediates, and the reaction of bromine with norbornene has been shown to lead to products consistent with a non-classical cationic species[89,90]. Evidence for the presence of these has not been noted either by myself or by others[67] for the reaction of phenylselenyl chloride with either norbornene or any 5-*exo* norbornene in a non-polar solvent.

This raises the problem of explaining *why* no rearrangement products are observed if the cation was significantly stabilised by a resonance donating group at C5. One possible explanation is that the cationic species attacked by the chloride ion at C3 is neither an open non-classical one such nor a selenium-bridged one, but one that has a structure somewhere between the two. It may be noted that the overall effect of any charge delocalisation over C5, C4, C3 and the Se would be to weaken the C3—Se bond, and make it easier for the chloride ion to cleave it by attacking C3. That such a structure could occur for addition of phenylselenyl chloride to norbornene but not bromine addition could be due to the seleniranium ring being more stable than one involving a bromonium ion.

If one considers the relative yields obtained and listed in Table 7 from a more quantitative point of view, there does appear to be some sort of a pattern.

Substituents that are generally recognised as having similar electronic effects as a result of their having related structures, e.g. Ac/CO_2Me/CO_2H, OH/OMe, and Cl/Br/I, tend to give, if not identical isomer distributions, at least reasonably similar ones. This is perhaps only what we would expect, given the likely absence of steric effects. However if we examine these groups more closely, a further trend emerges. If the substrates are listed in order of decreasing yield of the 3-chloro-2-phenylselanyl adduct (**58**), then with two exceptions (CN and phenyl) this order parallels remarkably well their Hammett σ^+_p or σ_p substituent constants (see Table 9)..

Table 9. Attack on C3 of 5-*exo*-X-2-norbornenes

X	% attack (C3)	log k_3/k_2	σ_I [a]	σ^+_p [a]	σ_p [a]
NH_2	100	?	+0.12	-1.3	-0.66
OH	90	0.95	+0.25	-0.92	-0.22
OMe	71	0.39	+0.34	-0.78	-0.27
H	50	0.00	0.00	0.00	0.00
OAc	47	-0.05	+0.38	-0.08[b]	+0.31
Cl	47	-0.05	+0.47	+0.11	+0.24
CN	47	-0.05	+0.57	+0.71[c]	+0.71
Br	44	-0.10	+0.47	+0.15	+0.26
I	41	-0.16	+0.42	+0.13	+0.28
Ac	36	-0.25	+0.28	+0.50[c]	+0.50
CO_2Me	31	-0.35	+0.31	+0.48[c]	+0.48
CO_2H	29	-0.39	+0.32	+0.42[c]	+0.42
Ph	25	-0.48	+0.10	-0.17	+0.05

[a] Unless otherwise indicated values are ones listed by N.S. Isaacs in *"Physical Organic Chemistry"*, 2nd ed, Longmans: Harlow, UK, 1995, pp152-3.

[b] A value closer to 0.0 may be more appropriate[91].

[c] Hammett σ_p value.

If this is more than coincidence, then it implies that the influence of resonance donors on the product ratio is quite considerable. The yield data are not really accurate enough for $\log k_2/k_3$ values to be used as a basis for a quantitative correlation, but some semi-quantitative assessments of the data can be made. The ones that encourage attack at C3 most are NH_2, OH and OMe, which have a relatively weak –I effect but are strong resonance donors. Those that cannot donate electrons by a resonance mechanism (Ac, CN, CO_2Me, CO_2H) all discourage attack at C3, presumably by virtue of their –I effect. A third group (OAc, Cl, Br, I, Ph) could be considered to have their polar and resonance effects more balanced, and they occupy an intermediate position (except in the case of Ph.).

Why should the presence of an electron withdrawing substituent at C5 discourage attack by chloride ion at C3? If X = H then the extent of any positive charge present on this carbon in the seleniranium intermediate generated as a result of the –I effect of the positively charged selenium will be the same as that on C2. However if there is an electron attracting substituent on C5 this will tend to discourage the development of such partial charges, and since it is closer, will affect C3 more than C2. Since the steric environment of C3 and C2 should be the same if the C5 substituent is an *exo* one, and the leaving group (PhSe) for attack at the two sites is identical, the chloride ion will be attracted to the carbon carrying the greater positive charge, which will be the C2 one. Consequently the presence of a –I group in the *exo* position of C5 should discourage attack by chloride ion at both C3 and C2, but at C2 least. Qualitatively this is what is observed for those substituents that are incapable of exerting a +M effect (CN, Ac, CO_2Me, and CO_2H).

Quantitatively, however, the extent of C3 attack found for the 5-exo-CN derivative looks far too high. The electron attracting ability of a cyano group is generally accepted to be considerably greater than that of any of the other substituents in the series, so one would expect that it should discourage attack at the C3 carbon the most. This anomalous behaviour on the part of CN, however, may not be as unusual as it appears. For example, in a study of the rates of

solvolysis of a series of 6-*exo*-X-2-*exo*-norbornyl tosylates Grob[92] found that the data correlated well with his polar substituent constants, but that two compounds (the 6-*exo*-F and 6-*exo*-CN) solvolysed abnormally rapidly. The rate of reaction for the 6-*exo*-CN derivative was comparable to that of the 6-*exo*-Br, and examination of the relative yields for these two in Table 7 shows that is also approximately true for phenylselenyl chloride addition. A similar anomaly had also previously been noted[93,94] in spectroscopic studies (^{13}C and ^{19}F) of the polar effect of the $-CH_2CN$ group. Whereas the value was normal in aromatic systems when it was *meta* to the probe site, it was abnormal when *para* to it. In both cases, as in Grob's work and the current investigation, it behaved as if it were more electron donating than expected, and had a value close to that of CH_2Br. There does not appear to be any such anomaly in either solvolysis of 6-*endo*-2-*exo*-norbornyl tosylates[83,92] or phenylselenyl chloride additions to 5-*endo*-2-norbornenes (see next section). This suggests that some form of hyperconjugative interaction involving the 5-*endo* H and an electron deficient C3 may exist. Although the distance between the two carbons is quite considerable (ca. 2.5Å) the geometrical alignment of the appropriate orbitals is excellent. Nevertheless in the absence of more evidence supporting this, such an explanation must be treated with considerable caution.

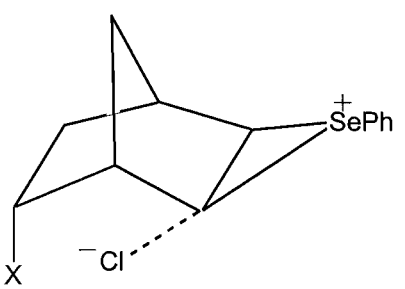
The other 'problem' substituent is the phenyl one. From an electronic point of view it would be expected to have little effect on the isomer ratio, i.e. the adducts should be formed in roughly equal yields. In spite of this it behaves as if it is electron withdrawing, and quite strongly discourages attack by chloride ion at C3. The result is about what would be expected had it been the *endo* alkene, but a careful examination of the NMR spectra of both the substituted norbornene[95,96] and the adducts confirmed that it was indeed the *exo* isomer.

It is interesting to compare the proposed interpretation of the effect of 5-*exo*-substituents with that observed by Goddard[81] for oxymercuration. In his system, the back lobe of the C5-X sigma bond is not prevented from interacting with any developing electron deficiency on C3, so Grob's proposed inductive mechanism for the transmission of the polar effect between C5 and C3 can

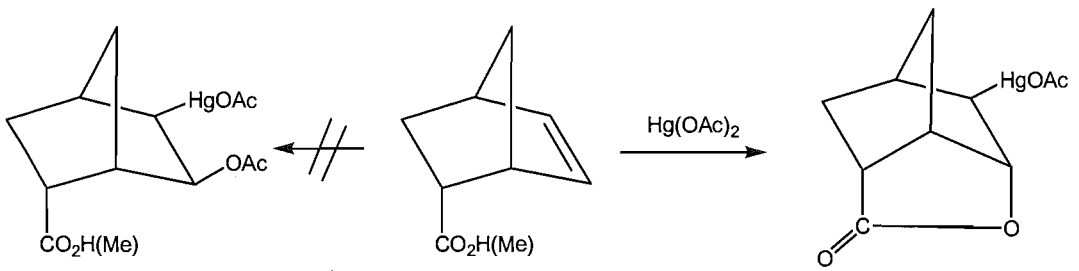
operate, just as it can for the solvolysis of his C6 and C2 *exo* tosylates. That, in contrast to mine, both Goddard's and Grob's results should be influenced mainly by the polar effect of X should therefore not be surprising. What is less clear, however, is the mechanism by which the bond between the incoming -OAc and C3 is formed. If this is S_N2, with retention of configuration, then it should still involve the same vacant orbital. It may be that the addition of mercuric acetate to norbornene is a concerted process.

3.2(iii) Reactions of 5-endo-Substituted-2-Norbornenes with Phenylselenyl chloride

The broad mechanistic features associated with the reaction of 5-substituted norbornenes with phenylselenyl chloride, i.e, the intermediate formation of a seleniranium ion and the exclusive formation of 2,3-adducts in which the phenylselanyl group is always *exo* and the chlorine *endo*, apply to both the 5-X-*exo*- and 5-X-*endo*-2-norbornenes. The introduction of a substituent into the 5-*endo* position as with the *exo*, introduces an asymmetry into the molecule, and as a result of this two isomeric 2,3-adducts can form. In the *exo* series their relative yields depended solely on the electronic effect of the 5-substituent — the orientation of the C-X bond in space precluded any significant steric interaction between X and a chloride ion attacking C3. In the 5-*endo*-series, however, this is no longer the case. The C5-C3 bond distance is not very great, and an *endo* X is very well placed to interfere with a chloride ion trying to attack the C2 from the opposite side to the C-Se bond.

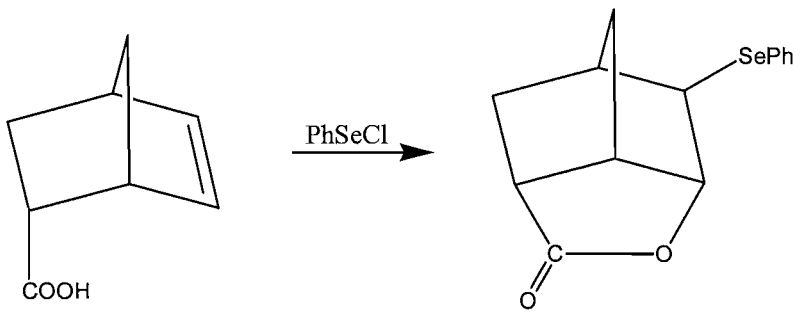


Some *endo* X groups have been shown to be capable of interacting sufficiently strongly with 2-norbornyl carbocations (or potential ones) to form covalent bonds to C3, particularly if such reaction leads to the formation of a 5-membered ring. For example, Factor and Traylor[97,98] have shown that, whereas oxymercuration of norbornene leads to a product in which both the HgOAc and OAc add to the *exo* face of the molecule, oxymercuration of both norbornene-5-*endo*-carboxylic acid and its methyl ester gives the lactone (**69**) as the sole product.



(**69**)

They also found that 5-*endo*-hydroxymethyl-2-norbornene under the same conditions gave a cyclic ether. Addition of PhSeCl to *endo* norbornene derivatives has been less studied, but Nicolaou[99-101] reported that addition to norbornene-5-*endo*-carboxylic acid gave the 2-phenylselanyl lactone[102] (**70**)



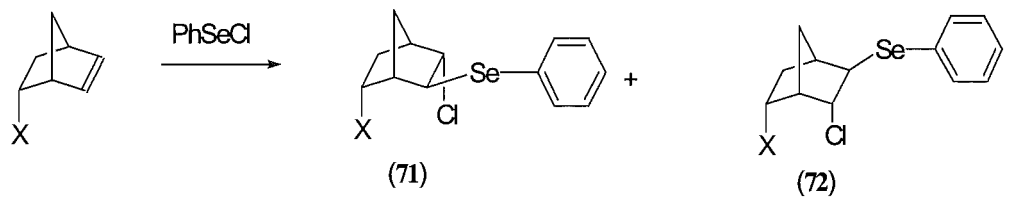
(**70**)

Of the range of 5-*endo* substituents included in my study,–CO_2H and -CO_2Me are structurally well suited to form (**70**) and –Ac and -OAc may at the very least interact strongly with a developing positive charge on C3. In addition –NH_2 and –OH might also be capable of interacting with this carbon. I found that

the *endo* –COOH derivative forms the lactone as the sole product, and the *endo*-CO_2Me forms it in 20% yield.

The ratios of the two adducts formed when phenylselenyl chloride was reacted with the 6-*endo*-norbornenes available are summarised in Table 10. (Values for the corresponding *exo* 2-norbornenes are given in parentheses.

Table 10. Relative yields of Adducts formed for Phenylselenyl chloride addition to 5-X-*endo*-2-Norbornenes.



X	**%**	**%**
NH_2[a]	100 (0)	0 (100)
OH	69 (10)	31 (90)
OMe[b]	91 (29)	9 (71)
H	50 (50)	50 (50)
OAc	67 (53)	33 (47)
CN	100 (53)	0 (47)
Ac[b]	100 (64)	0 (36)
CO_2Me	80 (69)	20[c] (31)
CO_2H	0 (71)	100[c] (29)

[a]The PhSeCl also reacts with the amino nitrogen of the starting material.

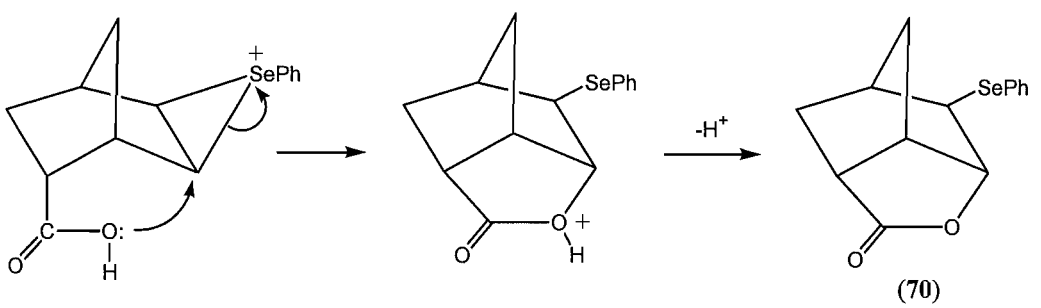
[b]Another unidentified product was also formed (see page 89)

[c]This product was the lactone (**70**)(see text).

The number of *endo* norbornenes investigated was smaller than in the 5-*exo* series. Those missing were X = Cl, Br, I, and C_6H_5. This was unfortunate because the first three are ones in which polar effects and resonance effects are

both quite strong, while the 5-*exo*-phenyl-2-norbornene gave an adduct ratio that could not be satisfactorily explained in terms of its electronic effect. (A product ratio for the *endo* phenyl compound could possibly have assisted in explaining the anomalous value obtained for the *exo* analogue.) The main reasons for the non-availability of these alkenes was that literature synthetic routes were either non-existent (X = I) or involved techniques/equipment unavailable in the department. Had they been crucial to the investigation, alternative routes would have been explored. However preliminary results in the *endo* series indicated that non-electronic factors were sufficiently important for the likely importance of the contribution of these to the body of data obtained to be insufficient to offset the effort required to make them.

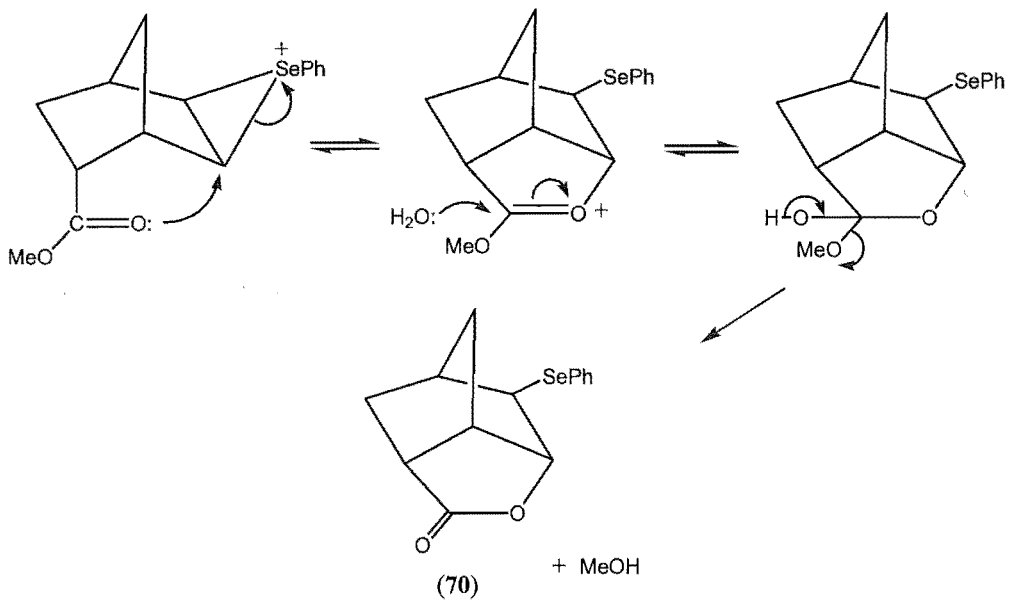
Inspection of the data in the table and comparison with that for the corresponding *exo* derivatives shows that the product distribution is affected by both the proximity and structure of the *endo* substituent. It is quite clear that in most cases the *endo*-X, with one exception, discourages nucleophilic attack at C3, presumably by virtue of its size. The only norbornene in which the main adduct was the product of nucleophilic attack on C3 of the seleniranium ion is the 5-*endo*-CO_2H one. In this case the lactone (**70**) is formed exclusively. Even here, though, this arises from a proximity effect, although of a different type.



(70)

There is one other case in which nucleophilic attack by the 5-*endo*-X-substituent on C3 definitely occurred, and this is with the 5-*endo*-CO_2Me compound. For this, although the major product has the expected structure, about

20% of lactone (**70**) is also formed. The most likely mechanism of lactone formation is shown on the next page.

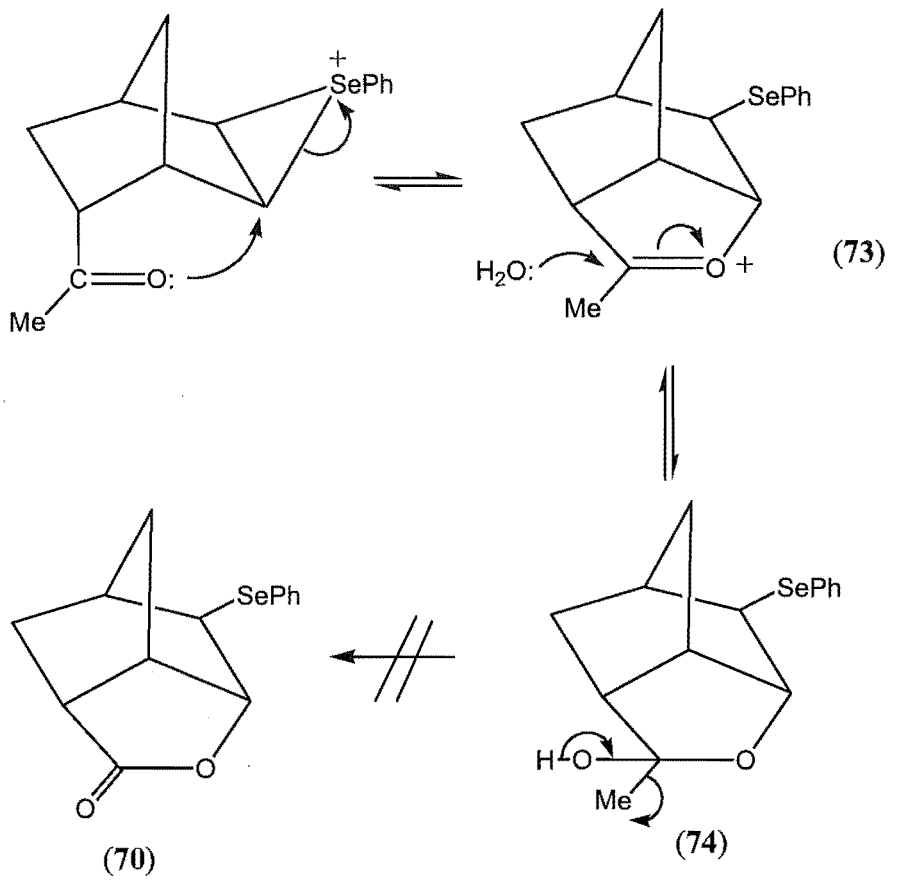


(**70**)

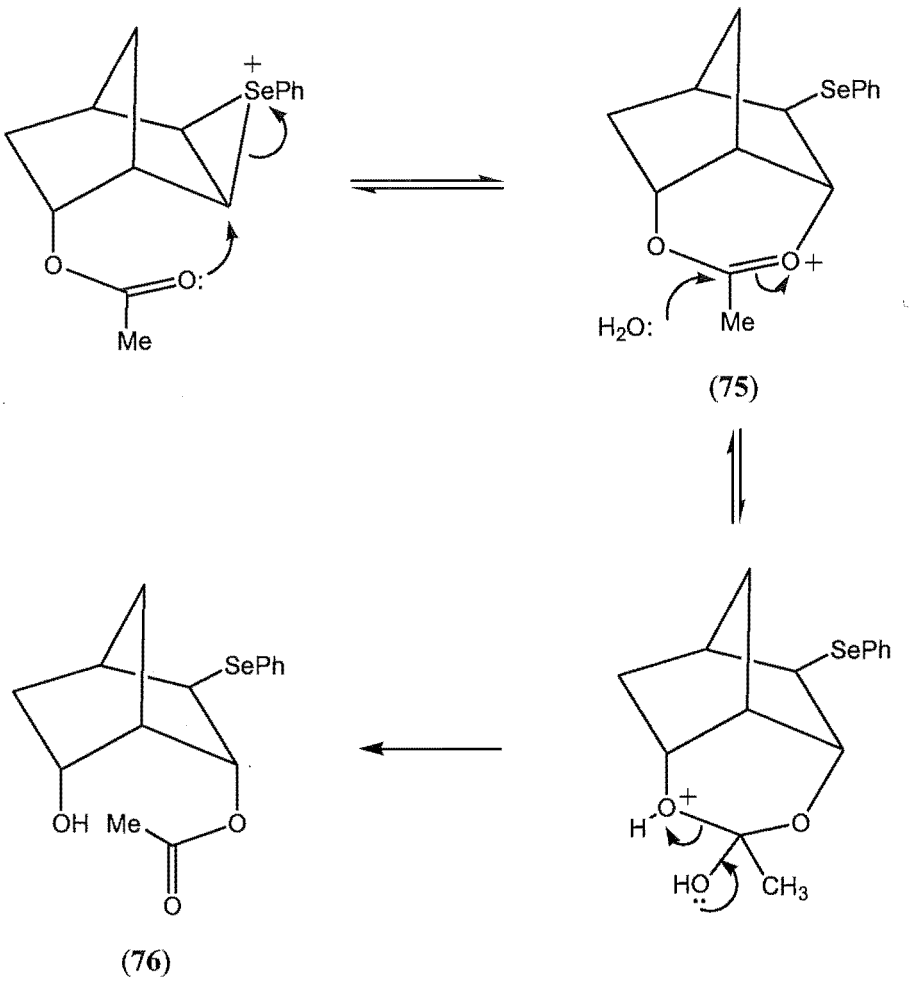
The C=O group of the ester group first attacks C3 and cleaves the seleniranium ring. This is followed by attack of a water molecule on this species to give (**70**). In theory there should be no water present, but in practice it would be difficult to exclude it entirely, and very little would be needed to produce the yield of (**70**) obtained. The above process must compete with attack by chloride ion at C2, which is favoured on electronic grounds, because the polar effect of the $-CO_2Me$ group will discourage the development of a positive charge on C3. That 80% of the total product is the result of chloride attack on C2, whereas with the 5-*endo*-CO_2H compound, no product of this origin is formed would seem unusual, since the electronic effects of the two substituents are very similar. The reason for the difference is probably that cleavage of the seleniranium ring by carboxyl attack at C3 is very fast, being strongly favoured on entropy grounds and almost certainly involves attack by the –OH group of the $–CO_2H$. For the $-CO_2Me$, in contrast, it will be the carbonyl oxygen that is the attacking nucleophile, and its addition to C3 would reversible. The total absence of any product arising from attack of chloride ion at C2 in the *endo* $–CO_2H$ is a little unexpected, since it represents about 30% of the total product in the *exo* isomer. The most likely explanation is a simple kinetic one. Attack by the carboxyl group is very fast, because its 'effective concentration' in the vicinity of C3 is very high. Another,

less likely, is a thermodynamic one. — An adduct of type (**73**) forms, but its formation is reversible, and during isolation of the product the chlorine is displaced by the carboxyl group to form the more stable lactone. This would seem improbable, though, as it requires nucleophilic attack on the same side of C3 as the chlorine.

In the light of the observed formation of a 20% yield of lactone (**70**) in the *endo* $-CO_2Me$ derivative, the situation with regard to the addition to the 5-*endo* – $COCH_3$ alkene is of interest. The acetyl group should resemble $-CO_2Me$ both electronically and sterically. The first step, reversible attack by the carbonyl oxygen on C3 to give (**73**), can and probably does occur. However the second, addition of a water molecule to the carbonyl carbon, would lead to the hemiketal (**74**) and this is unlikely to be stable under the conditions. Nevertheless, the formation of either may serve to block access to C3 by the chloride ion, and prevent the formation of adduct of the type (**72**). One possible piece of evidence in support of the formation of (**73**) or the (**74**) is the observation that the initially formed product mixture appears to contain about 10% of a compound that decomposed too rapidly for it to be identified.



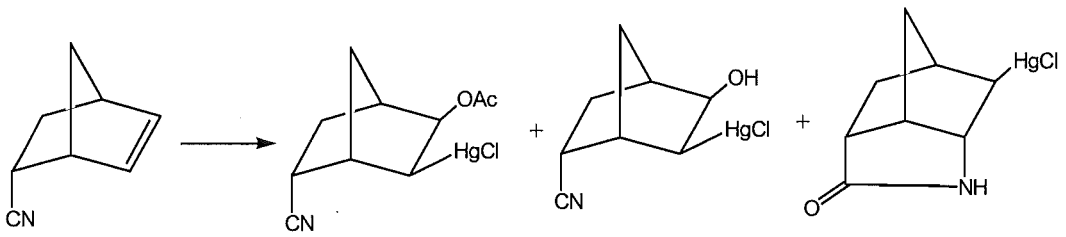
The other *endo* norbornene for which interaction with C3 should be possible is the 5-*endo*-OAc derivative. However this compound appeared to react to give the expected mixture of phenylselenyl chloride adducts. Oxymercuration of this compound also gives normal 5-*endo*-acetoxy products[81] so perhaps this is to be expected. Interaction with the C=O oxygen of the acetate to give (**75**) should be possible: Subsequent attack by a water molecule in this case should give the 5-*endo*-hydroxy ester (**76**).



That (**76**) is not formed as a product means that either a 6-membered ring does not form as readily as a 5-membered one, or that if it does, its formation is reversible, and the hydrolysis step is slow. Probably both factors contribute, with the second being the more important. Hydrolysis of the CO_2Me derivative to give (**70**) involves the hydrolysis of the ester of a primary alcohol (methanol), while hydrolysis to give (**75**) is hydrolysis of a secondary alcohol and this would be a much slower process. It is interesting to note that, unlike an *endo* $-CO_2Me$ substituent, an *endo* –OAc one does not suppress attack of chloride ion on C3. This probably means that the position of the first equilibrium favours the starting material, and the amount of (**75**) present is low.

The other *endo* compounds studied also bear substituents that are capable of interfering with *anti* attack of a chloride ion at C2 of the seleniranium ion. Three of them, $-NH_2$, -OH, and -OMe are nucleophilic, and could, in theory

interact with an electrophilic C3. However the result in each case would involve the formation of a 4-membered ring, and these are never very stable. No [2.2.1]bicycloheptane system in which C3 and C5 are bridged by O or N has ever been reported, so presumably they would not compete very effectively with chloride ion. Any proximity effect arising should be therefore mainly a 'size' one. The remaining norbornene studied, the *endo* 5-CN derivative, could also fall into this category, although as a nucleophile, it would be very weak one. Factor and Traylor[97,103] investigated the oxymercuration of 6-*endo*-cyano-2-norbornene and found evidence for the formation of lactam (**77**) in addition to the normal oxymercuration products.



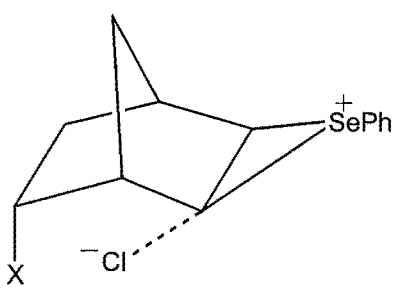
(77)

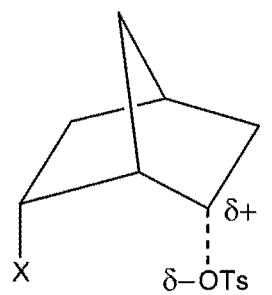
However they were unable to confirm its structure. From a geometric point of view, the lone pair of the –CN group would be directed away from C2, and therefore unlikely to interact with it during the reaction. If (**77**) was indeed formed, then it would be far more likely to be as a result of oxymercuration of some 5-*endo*-$CONH_2$ formed as a result of hydrolysis of the nitrile (a process possibly catalysed by mercuric ion). Of all the *endo* alkenes used in my study, the cyano compound is least likely to sterically hinder attack by chloride ion at C3, as it is small, comparable in size to a halogen such as Cl or Br.

The discussion so far has concentrated largely on the effect of an *endo* substituent on C5's proximity to C3 on the subsequent reaction of the phenylseleniranium cation at this carbon. The main reason is that until some understanding of this is gained, it is difficult to consider the electronic effect of X. Viewed electronically, all of the *endo*-X studied are electron withdrawing by a polar mechanism. All are also either resonance donors or resonance withdrawers. The bottom four in Table **10** (-CN, -Ac, $-CO_2Me$, and $–CO_2H$) must be electron withdrawing overall, because both their polar and resonance effects operate in the

same direction. With the exception of -CO_2H, (for which proximity effects appear to dictate the product formed) all favour formation of an adduct of type (**71**), i.e. the one where the chloride ion attacks the carbon more distant from X (C2) rather than the closer one (C3). While this could be explained in terms of a simple steric effect due to the size of X, it is also in accord with X's electron attracting character, which would tend to discourage the development of positive charge on the nearer carbon. There is, in fact, no evidence for the formation of any product arising from attack by chloride ion at C3 of the phenylseleniranium ion with these four substituents.

Grob[104] has studied the rates of solvolysis of a number of 6-*endo*-X-2-*exo*-norbornyl *p*-toluenesulfonates and 6-*endo*-X-2-*endo*-norbornyl *p*-toluenesulfonates. Data from these studies were available for comparison purposes for five of our substituents (OH, OMe, OAc, CN, and CO_2Me) in the first series and for the first four of these in the second. The first of Grob's series represents a system that reflects the effect of the electronic effect of X on the stability of a developing charge on C2, as an *exo* group leaves as an anion. The second differs only in that this time the departing group is an *endo* one. The second corresponds more closely to my system — the transition state for the departing tosylate ion bears some degree of resemblance to that for attack of chloride ion at C3 of a 5-*endo* compound.





A comparison of the proportions of adduct (**72**) formed in my PhSeCl addition to the 5-X-*endo*-3-norbornenes and the corresponding relative rate data for the solvolysis of Grob's 5-*endo*-X-*exo*- and 6-*endo*-X-*endo*-2-norbornyl tosylates in 80% ethanol is given in .**Table 11** (next page).

Table 11. Relative Rates of Solvolysis of 6-*endo*-X-2-*exo*-norbornyl and 6-*endo*-X-2-*endo*-norbornyl *p*-toluenesulfonates and yields of (**72**) in addition of C_6H_5SeCl to 5-*endo*-X-norbornenes

X	k_{rel}(exo)[a]	k_{rel}(endo)[b]	k_3^X/k_2^X [c]
OH	6.6×10^{-3}	5.6×10^{-2}	0.45
OMe	2.5×10^{-3}	7.7×10^{-2}	0.10
H	1	1	1
OAc	1.6×10^{-3}	4.6×10^{-3}	0.49
CN	1.2×10^{-6}	1.6×10^{-4}	≈0
CO_2Me[d]	8.4×10^{-2}		0.25

[a] $k_{rel}(exo) = k^X/k^H$ for solvolysis of 6-*endo*-X-2-*exo*-norbornyl *p*-tosylate at 70° in 80% ethanol.

[b] $k_{rel}(endo) = k^X/k^H$ for solvolysis of 6-*endo*-X-2-*endo*-norbornyl *p*-tosylate at 140° in 80% ethanol.

[c] k_3^X/k_2^X is the ratio of the yields of adduct (**72**) to adduct (**71**) formed in PhSeCl addition.

[d] The product of reaction at C3 are lactones.

The data in the first column provide the best guide to the role played by electronic effect in the systems. Significant neighbouring group interactions between X and C3 will still be present in some cases. Grob found that there was interaction between both *endo* -CO_2Me and -OAc groups and the developing charge on C2 as the former yielded a lactone and the latter an *endo* diol monoacetate as reaction products. (This probably explains the unusually high reaction rate for their *endo*- 6-CO_2Me derivative; as such interaction could assist the departure of the tosylate.). The second column corresponds to a situation where the substituent X would find it difficult to interact with the developing charge on C2 because the tosylate would be in the way. However if it was large, it could influence the reaction rate by interacting with the departing tosyl group or affecting its solvation. The third column (my data) should to some extent have element of both of the first two. Some groups can potentially interact with a partially positively charged C3 as in column 1, and in doing so compete with, or prevent, a chloride ion from doing so. (Others may not). On the other hand,

interactions of the type expected in column 2 would affect access to C3, by chloride ion, and possibly affect its nucleophilicity.

The data for the product ratios obtained for the PhSeCl additions are much less reliable than that from the kinetic studies, and the number of substituents rather small, so quantitative correlations would not be very meaningful. The best way of assessing the importance of the various factors is to consider the orders or reactivity of the various substituents.

For solvolysis of the 6-*endo*-X-2-*exo*-norbornyl tosylates:

H > OAc > OMe > OH >> CN

For solvolysis of the 6-*endo*-X-2-*endo*-norbornyl tosylates:

OH >H >OMe >OAc > CN

For formation of 5-*endo*-X-3-*endo*-chloro-2-phenylselanylnorbornane:

H > OAc ≈OH > OMe>> CN

With the exception of OH in the solvolysis of 6-*endo*-X-2-*endo*-norbornyl tosylates the order is remarkably similar in all three. Grob attributed the anomalously high reactivity of the 6-*endo*-hydroxy-*endo*-norbornyl tosylate to intramolecular hydrogen bonding involving the –OH assisting the departure of the tosylate group, and lowering the energy of the transition state for the solvolysis.

For comparison, the corresponding orders for the 6-*exo*-X series are:

For solvolysis of the 6-*exo*-X-2-*exo*-norbornyl tosylates:

H > OH ≈ OMe >> OAc > CN

For solvolysis of the 6-*exo*-X-2-*endo*-norbornyl tosylates:

OH ≈H >OMe >OAc > CN

For formation of 6-*exo*-X-2-*endo*-chloro-3-phenylselanylnorbornane:

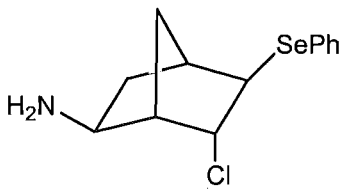
OH > OMe > H ≈OAc >> CN

Grob found that the rate data for the two 6-*exo*-X tosylate series gave (except for OH in the *endo* tosylate one) good correlations with the polar

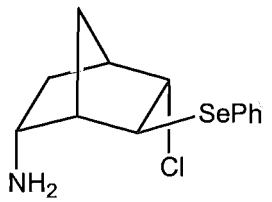
substituent constants, whereas my results for PhSeCl addition to the 6-*exo*-X norbornenes suggested that in this reaction there was a significant contribution from resonance effects when X was a resonance donor. In the 6-*endo*-X series, Grob also observed acceptable correlations with polar substituent constants in both solvolyses. My data for PhSeCl addition to 5-*endo*-X-norbornenes, also indicated that yields of the 3-Cl adduct roughly paralleled the polar effect of X (the data are not really reliable enough for quantitative correlations), but that, unlike the corresponding 5-*exo*-X-2-norbornene addition, resonance donors did not encourage attack by chloride ion at C2.

There are three 5-*endo*-X-substituted 2-norbornenes that I studied for which no rate data on the corresponding 2-*exo* and 2-*endo* tosylate solvolyses are available. Grob looked at the 6-*endo*-CO_2H compound, but found that the rate was too fast to measure. This would suggest that neighbouring group participation by this substituent was assisting the reaction. Given this, that addition of PhSeCl to 5-*endo*-CO_2H-2-norbornene gives exclusively the lactone as a product should not therefore be too surprising. The other two (X = Ac and X = NH_2) Grob did not prepare and study. However my finding that addition to the 5-*endo*-acetyl alkene gave a single adduct, with structure of type (**71**) (i.e. the chloride attacked only C2) is consistent with the result for the result for X = CN, which is of similar electronic character and gave a similar result. The result obtained for the remaining substrate (X = NH_2) posed problems. As has been noted previously, PhSeCl reacts with the double bond of norbornene at a rate comparable to that at which it reacts with a primary amine. As a result, reaction with both 5-amino-2-norbornenes gave a mixture of one of the adducts and the corresponding 5-phenylselanylamino-2-norbornene as products. Of considerable interest was the fact that (a) only one of the two possible adducts was formed in each case, (b) the adducts in the *exo* and *endo* series had opposite orientations, and (c) there was no sign that the alkene ever reacted with two molecules of PhSeCl to give an *N*-phenylselanylated adduct as a product in either reaction.

With regard to (a), this was not too surprising in so far as the 6-*endo*-amino-2-norbornene was concerned. The adduct formed was 6-*endo*-amino-2-*endo*-chloro-3-*exo*-phenylselanylnorbornane (**78**)



(**78**)



(**79**)

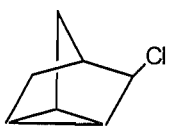
The absence of the other adduct was not unexpected, as 5-*exo*-hydroxy-2-norbornene and 5-*exo*-methoxy-2-norbornene gave mainly the analogous product and the results overall suggested this was favoured by the presence of a strong resonance donor in the *exo* C5 position. However the exclusive formation of adduct (**79**) of opposite orientation, from 5-*endo*-amino-2-norbornene was unexpected. The 5-*endo*-acetyl and 5-*endo*-cyanonorbornenes also yielded a single adduct with this orientation. Such behaviour on the part of the last two is consistent with orientation being influenced by the polar effect of the substituent, (both are strongly electron withdrawing) but an amino group is only weakly electron withdrawing. As we have noted, in the *exo* series a strong resonance donor such as NH_2 favours the formation of the adduct with the Cl at C3, but there is clearly no such factor operating in the *endo* series. At the present time I can offer no explanation for this result.

Chapter 4

CRYSTAL STRUCTURES OF SOME 5-X-SUBSTITUTED-NORBORNENES

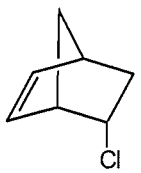
4.1 Introduction

In 1954 Roberts and Bennett[105] reported the results of a study of the rates of solvolysis of the chlorides below in 80% ethanol-water at 85°.



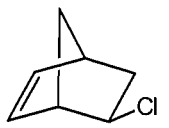
(80)

0.019 hr^{-1}



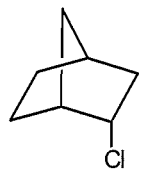
(81)

<0.005 hr^{-1}



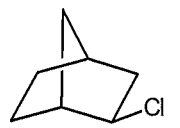
(82)

0.078 hr^{-1}



(83)

~0.002 hr^{-1}

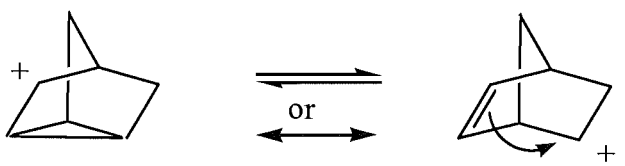


(84)

0.14 hr^{-1}

Inspection of the data shows that the 2-*exo*-norbornyl compound (**84**) reacts fastest and the 2-*endo*-norbornyl and 2-*endo*-norbornenyl derivatives ((**83**) and (**81**) respectively) react the slowest. The nortricyclyl chloride (**80**) solvolyses at a rate comparable to that of cyclopentyl chloride. On this basis (**84**) and (**82**) appear to both be solvolysing abnormally rapidly, and the fact that they are both reacting much faster than their *endo* analogues suggests that the loss of chloride is enhanced by participation of the norbornane skeleton. In the case of the 2-norbornyl compound, solvolysis presunmably occurs by an S_N1 mechanism to give the non-classical norbornyl cation and is assisted by the enhanced stability arising from electron delocalisation involving the electrons of the C1-C6 bond in this species. For the 2-norbornenyl compound stabilisation is slightly less, and the acceleration was attributed to participation by the π electrons of the C=C bond in some way.

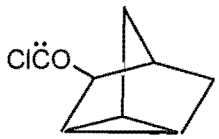
These results supported earlier data obtained by Winstein[5,6] for the solvolysis of the corresponding *p*-bromobenzenesulfonates in acetic acid, where he reported that the relative rates of solvolysis of the compounds analagous to (**80**), (**82**) and (**81**) were 2000:7000:1. Neither group reported the compositions of their products, but since at that time neither separation methods such as high performance liquid chromatography nor identification by NMR techniques were available, this was perhaps not surprising. Subsequent work by Roberts[106] and Cristol[107] established that both the 2-norbornenyl and nortricyclyl compounds of these types yielded mixtures of 2-norbornenyl and nortricyclyl derivatives on solvolysis, with the latter predominating. The formation of both types can be explained by assuming a facile equilibrium between the two cations exists. However it is also possible that (**85**) and (**86**) represent resonance forms of a non-classical cation.

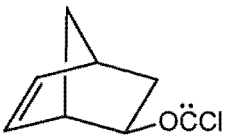


(**85**) (**86**)

The bulk of the early evidence favoured an equilibrium, with (**85**) being the major species present, but later low temperature NMR studies by Olah[108,109] and by Saunders[110] suggested that a single species was involved, that it resembled (**85**), but that there was some charge delocalisation into the cyclopropane ring — in other words, it was a non-classical species. One of the problems with this interpretation was that the nortriclyl/norbornenyl product ratios varied with the reaction conditions. This was, however, attributed to factors such as solvation.

Recently Moss[111] generated (**85**) and (**86**) independently from the oxychlorocarbene precursors (**87**) and (**88**).





(87) **(88)**

Fragmentation led to the formation of a mixture of chlorides, with the actual composition depending on the solvent. (see below)

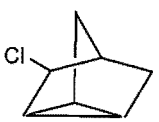
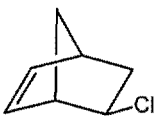
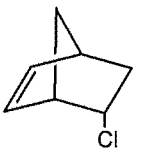
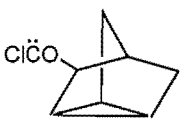
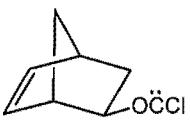
Precursor	**Solvent**			
	pentane	100%	0%	0%
	1,2-dichloroethane	89.2%	10.8%	0%
	acetonitrile	89.9%	10.1%	0%
	pentane	16.4%	56.1%	27.5%
	1,2-dichloroethane	32.4%	67.6%	0%
	acetonitrile	43.0%	57.0%	0%

Figure 35. Products from fragmentation of **(87)** and **(88)** in various solvents

They also obtained data for the fragmentations in methanol and found that in this solvent the bias towards formation of methyl ethers strongly favoured nortricyclyl products over 2-*exo*-norbornenyl ones.

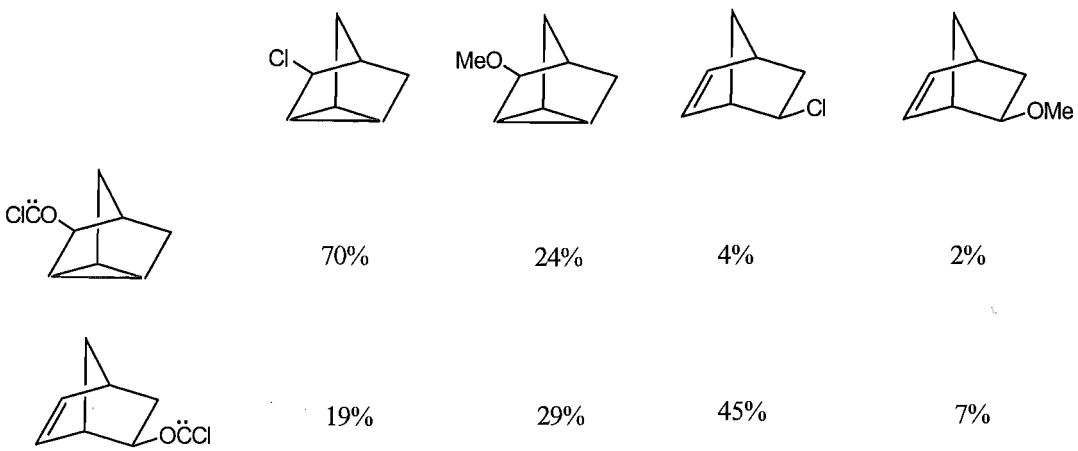


Figure 36. Products from fragmentation of (**87**) and (**88**) in methanol

Their interpretation was that, in pentane, chloride formation involved an S_Ni-like process, although perhaps very tight ion-pairs might be short lived intermediates. However in polar solvents the ion-pairs were longer lived. The relative yields of the two methyl ethers in methanol, together with the absence of 2-*endo*-norbornenyl products is consistent with the formation of an ion-pair consisting of a non-classical cation associated with a chloride ion. The non-classical cation resembles nortricyclyl more than norbornenyl (i.e. (**85**) more than (**86**)) but as in pentane, there is a tendency for the chloride ion to react at the positively charged carbon that is the nearer to it at the time it forms. This tendency also remains for ether formation, but is much lower. Consequently much less 2-methoxynorbornene is formed from the nortricyclyl precursor (**87**) than methoxynortricyclene from the norbornenyl one (**88**). Such a 'memory' effect had not been observed in the previous solvolysis studies of Roberts[5] and of Cristol[107].

The stabilisation of a positive charge on C5 of a 2-norbornene skeleton involves interaction of the π system of the double bond with the electron deficient centre. That such interaction is quite considerable is indicated by the strong tendency of the products obtained from it being nortricyclyl ones. If there is no electron deficiency at C5, interaction should not occur. However if there is an *exo* substituent (X) on C5 the electrons of the π system are stereochemically well

placed to overlap with the σ* orbital of the C-X bond (a $n_\pi \rightarrow \sigma^*$ interaction). Such an interaction is well established in carbohydrate chemistry in the form of the anomeric effect, although in that case it is of the $n_\sigma \rightarrow \pi^*$ type, and involves lone pairs on the oxygen of a pyranose ring. The strength of the interaction depends on the electronegativity of X, increasing as the latter rises. When X is an oxygen, the strength depends on how electron attracting the group attached to it is. Such an interaction has been shown by Kirby and co-workers to affect the length of the C-O bond to an extent that can be detected by X-ray structure determination[112-114]. White and Robertson[115] have shown that in 4-*t*-butylcyclohexyl esters the introduction of a $SiMe_3$ group has relatively little effect on the length of the C-O bond unless the two bear an antiperiplanar relationship, i.e both occupy axial sites. In the latter case it is significantly longer than normal.

Bentley and co-workers have carried out a kinetic study of the solvolyses of some 6-trimethylsilyl-*exo* and *endo*- norbornyl esters[116] and found that, when the ester was *exo*, both the *exo* and *endo* $SiMe_3$ groups enhanced the rate considerably with the effect of the *exo* $SiMe_3$ being about 100-fold greater. However when the ester group was *endo*, the rate acceleration was much less for the *exo* $SiMe_3$ and an *endo* $SiMe_3$ retarded the reaction. The abnormal enhancement of the rates when an *exo* $SiMe_3$ was present in the 6-position was atttributed to an interaction between back lobe of the C-Si bond and the developing electron deficiency at C2, rather than hyperconjugative stabilisation. In such circumstances it is a little surprising that the electrons of the double bond of a norbornene are capable of interacting with orbitals on C2. However a vinyl group is a better resonance donor than $-CH_2SiMe_3$, and in the rigid norbornyl system any interaction would be encouraged by the π electrons being sterically constrained to a position well suited for this. It is interesting to note, (but not really relevant) that both Roberts and Winstein found that *exo*-2-norbornyl esters solvolysed about twice as fast as the corresponding *exo-2*-norbornenyl ones, which indicates that stabilisation of the developing positive charge by the C1-C6 bond in the saturated system is greater than stabilisation by C5-C6 π electrons.

In the past, systematic studies of variations in bond lengths derived from X-ray structure determinations have not been used as a means of assessing electronic interactions between adjacent parts of molecules. The barriers to this have been technological ones. Until relatively recently the determination of molecular structures by X-ray methods was relatively time consuming, and the data obtained, while satisfactory for determination of the gross molecular structures , was often not of sufficient precision for small differences to be reliably established. However in recent years, the technology for the collection of data at low temperatures has led to both data collection times being considerably reduced, and the data obtained being of much higher quality. The result has been that investigations aimed at establishing trends in bond lengths over a range of closely related compounds where the differences observed may be quite small and today can constitute an acceptable approach from both economic and practical points of view. Unfortunately while the technological constraints have been removed, there are still ones of a practical chemical nature that have proved less easy. In particular, no matter how good the instrumentation, the quality of the data obtained is highly dependent on the quality of the crystals that are its source. While the skills of the person obtaining these can be of considerable help, there are some cases where problems are still encountered. Perhaps the most common of these is disorder in the arrangement of the molecules in the crystal. These are most commonly arise when the molecules are compact and of roughly spherical shape, because in such circumstances changes in orientation within the crystal involve only small changes in energy. If such disorder occurs, it is often sufficiently small that the ability to 'solve' the structure is not affected. However the accuracy with which bond lengths can be obtained will fall off. If this happens it becomes very difficult to determine whether an observed difference in length is indeed real, or whether it is simply the result of the use of a poor crystal. Although unanticipated at the time, it turned out that the roughly spherical shape of the norbonene skeleton led to considerable disorder occurring in many of my crystals with the result that the quality of the data I obtained being less than I had hoped.

The compounds prepared for X-ray crystallographic study were:

exo-bicyclo[2.2.1] hept-5-en-2-yl 4-nitrobenzoate

endo-bicyclo[2.2.1] hept-5-en-2-yl 4-nitrobenzoate

exo-bicyclo[2.2.1]hept-5-en-2-yl 3,5-dinitrobenzoate

endo-bicyclo[2.2.1] hept-5-en-2-yl 3, 5-dinitrobenzoate

exo-bicyclo[2.2.1]hept-5-en-2-yl 4-bromobenzenesulphonate

endo-bicyclo[2.2.1]hept-5-en-2-yl 4-bromobenzenesulphonate

exo-bicyclo[2.2.1] hept-5-en-2-yl 3-nitrobenzoate

exo-bicyclo[2.2.1] hept-5-en-2-yl 3-nitrobenzenesulphonate

exo-bicyclo[2.2.1]hept-5en-2-yl 4-nitrophenylether

A more extensive range of compounds was planned originally, but for reasons discussed in the following section the study was halted before it was completed.

4.2 RESULTS AND DISCUSSION

The preparation of the 5-norbornenyl esters is given in the Experimental section of this thesis. All measurements were made with a Siemens CCD area detector using graphite monochromatised Mo Kα (λ = 0.710730A°) radiation at the temperature indicated in Tables A1 and A2. The data reduction was performed using SAINT.[117] Intensities were corrected for Lorentz and polarisation effects and for absorption using SADABS[118]. Space groups were determined from systematic absences and checked for higher symmetry. The structures were solved by the direct method using SHELXS[119] and refined on F2 using all data by full matrix least-squares procedures with SHELXL-97[120]. All non hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions with isotropic displacement parameters 1.3 times the isotropic equivalent of their carrier carbons. Absolute structure determinations were on Flack parameter. The functions minimised (∑ww(F02 – Fc2)o,with ww=[σ2 F02)+(aP2)+(Bp)-1,where P=[max(F0)2 + 2 Fc2]/3. In all cases final Fourier synthesis showed no significant residual electron density in chemically sensible positions.

Only selected bond lengths and angles will be discussed in this section. The remaining distances and angles, as well as atom coordinates, anisotropic displacement parameters and hydrogen atom coordinates are available from the University of Canterbury chemistry department.

The Crystal and X-Ray experimental data are summarised in Table A1 and A2 on the next two pages.

Table A.1. Crystal data and X-ray experimental data for 4.5, 4.6, 4.7, 4.8, 4.9.

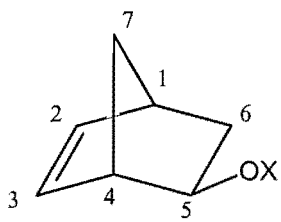
Compound	4.5	4.6	4.7	4.8	4.9
Empirical formula	$C_{14}H_{13}NO_4$	$C_{14}H_{13}NO_4$	$C_{13}H_{13}BrO_3S$	$C_{13}H_{13}NO_3$	$C_{14}H_{12}N_2O_6$
Formula weight	259.25	259.25	329.20	231.24.,	304.26
Temperature (K)	168(2)	93(2)	205(2)	93(2).,	158(2)
Crystal system	Monoclini	Triclinic	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1/c$	P-1	$P2_1/c$	$P2_1/n$	P-1
Unit cell dimensions: a (Å)	9.534(3)	6.7577(13)	9.9438(9)	5.7874(9)	6.329(8)
b (Å)	9.918(4)	8.2374(17)	11.5916(11)	21.352(4)	9.563(13)
c (Å)	13.447(5)	11.572(2)	12.2806(11)	9.0491(15)	11.857(16)
α (°)	90	106.961(4)	90	90	87.171(15)
β (°)	97.063(5)	91.329(4)	110.237(1)	98.628(3)	70.647(14)
γ (°)	90	97.840(4)	90	90	84.59(3)
Volume ($Å^3$)	1261.9(8)	609.0(2)	1328.1(2)	1105.6(3)	673.9(15)
Z	4	2	4	4	2
Density (calculated)(Mg/m^3)	1.365	1.414	1.646	1.389	1.499
Absorption coefficient (mm^{-1})	0.101	0.105	3.249	0.099	0.119
F(000)	544	272	664	488	316
Crystal size (mm^3)	0.53 x 0.51 x 0.39	0.44 x 0.24 x 0.03	0.75 x 0.50 x 0.05	0.60 x 0.42 x 0.12	0.60 x 0.14 x 0.06.
Theta range for data collection(°)	2.15 to 25.00	1.84 to 26.38	2.49 to 26.44	1.91 to 26.41	1.82 to 26.34
Reflections collected	14390	5083	9107	8590	3282
Independent reflections [R(int]	2214) [0.0191]	2366[0.0441]	2582[0.0324]	2216[0.0563]	2498[0.1232]
Observed reflections [I>σ(I)].	1608	1497	2071	1388	349
Data/restraints/parameters	2214/0/208	2366/0/172	2582/0/163	2216/0/154	2498/0/199
Goodness-of-fit on F^2	1.056	1.040	1.046	0.992	0.564
R_1 [I>2σ(I)]	0.0553	0.1029	0.0534	0.0534	0.0498
wR_2 (all data)	0.1459	0.2863	0.1329	0.1030	0.0855

Table A.2. Crystal data and X-ray experimental data for 4.11, 4.12, 4.13, 4.14,.

Compound		4.11	4.12	4.13	4.14
Empirical formula		$C_{13}H_{13}BrO_3S$	$C_{14}H_{13}NO_4$	$C_{14}H_{12}N_2O_6$	$C_{13}H_{13}NO_5S$
Formula weight		329.20	259.25	304.26	295.30
Temperature (K)		273(2)	93(2)	163(2)	183(2)
Crystal system		Monoclinic	Monoclinic	Monoclinic	Monoclinic
space group		$P2_1/c$	$P2_1/c$	$C2/c$	$P2_1/c$
Unit cell dimensions	a (Å)	10.016(3)	8.702(4)	26.503(13)	8.224(5)
	b (Å)	11.770(3)	12.354(5)	5.845(3)	9.217(6)
	c (Å)	11.870(3)	11.306(4)	17.460(9)	17.032(11)
	α (°)	90	90	90	90
	β (°)	108.881(2)	106.011(7)	94.469(6)	100.29(10)
	γ (°)	90	90	90	90
Volume (Å^3)		1 324.0(6)	1168.4(8)	2697(2)	1270(14)
Z		4	4	8	4
Calculated density (Mg/m^3)		1.652	1.474	1.499	1.544
Absorption coefficient(mm^{-1})		0.113	0.109	0.119	0.275
F(000)		664	544	1264	616
Crystal size (mm^3)		1.00 x 0.47 x 0.05	0.72 x 0.42 x 0.08.	0.70 x 0.11 x 0.025	0.50 x 0.50 x 0.40
Theta range for data collection (°)		2.15 to 26.26	2.43 to 26.44	2.34 to 26.48	2.43 to 26.64
Reflections collected		16213	9206	14071	6303
Independent reflections[R(int)]		2667[0.0267]	2383[0.0868]	2714[0.1767]	2547[0.0267]
Observed reflections [I>2σ (I)]		2167	1404	732	2147
Data / restraints / parameters		2667/0/163	2383/0/172	2714/0/199	2547/0/181
Goodness-of-fit on F^2		1.049	1.020	0.818	1.050
R_1[I>2σ (I)]		0.0970	0.0776	0.0728	0.0517
wR_2 indices (all data)		0.2661	0.1410	0.1809	0.1367

The R factors obtained are on the high side for the degree of accuracy in bond lengths that I had hoped to obtain, but these are not recognised as particularly good indicators of the reliability of the calculated C-C, C=C and C-O bond lengths in the molecule. The values of these for all of the compounds for which I obtained data are summarised below in Tables 12 and 13.

Table 12. Summary of C-C, C=C and C-O Bond lengths for the Norbornyl skeleton of some *exo* norbornyl esters.



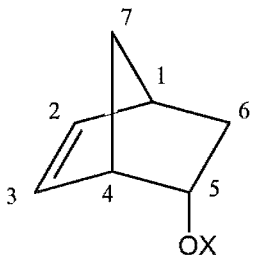
4.5 X = *exo*-4-nitrobenzoate 4.6 X = *exo*-3-nitrobenzoate

4.7 X = *exo*-4-bromobenzenesulfonate 4.8 X = *exo*-4-nitrophenoxy

4.9 X = *exo*-3,5-dinitrobenzoate

Bond	4.5	4.6	4.7	4.8	4.9
O1-C5	1.467(3)	1.450(6)	1.486(6)	1.444(3)	1.486(8)
C1-C2	1.529(8)	1.503(10)	1.562(9)	1.484(12)	1.448(12)
C2-C3	1.130(6)	1.366(10)	1.284(9)	1.326(4)	1.313(12)
C3-C4	1.538(9)	1.455(10)	1.530(9)	1.493(4)	1.444(13)
C4-C5	1.702(10)	1.535(10)	1.549(8)	1.542(3)	1.551(10)
C5-C6	1.467(3)	1.524(7)	1.550(7)	1.526(3)	1.495(10)
C1-C6	1.520(12)	1.486(10)	1.479(8)	1.542(4)	1.455(11)
C4-C7	1.521(11)	1.699(12)	1.546(9)	1.534(4)	1.666(12)
C1-C7	1.538(8)	1.405(12)	1.469(9)	1.523(4)	1.511(13)

Table 13. Summary of C-C, C=C and C-O Bond lengths for the Norbornyl skeleton of some *endo* norbornyl esters.



4.11 X = *endo*-4-bromobenzenesulfonate 4.12 X = *endo*-4-nitrobenzoate

4.13 X = *endo*-3,5-dinitrobenzoate 4.14 X = *endo*-3-nitrobenzenesulfonate

Bond	4.11	4.12	4.13	4.14
O1-C5	1.450(13)	1.437(4)	1.473(7)	1.474(9)
C1-C2	1.350(3)	1.511(6)	1.516(14)	1.483(8)
C2-C3	1.320(3)	1.299(6)	1.170(3)	1.344(8)
C3-C4	1.410(2)	1.473(6)	1.743(17)	1.485(8)
C4-C5	1.475(16)	1.508(5)	1.523(9)	1.522(8)
C5-C6	1.800(3)	1.512(6)	1.503(9)	1.533(8)
C1-C6	1.370(2	1.512(6)	1.517(10)	1.538(7)
C4-C7	1.468(19)	1.526(6)	1.523(11)	1.578(8)
C1-C7	1.830(2)	1.493(6)	1.267(12)	1.493(8)

The numbers given in parentheses represent the standard deviations in the last digit of the calculated lengths, e.g. 1.529(8) means a standard deviation of 0.008 in the distance determined (1.529Å). The advice of experienced workers in this field was that in almost all cases the standard deviations obtained were so high as to make it unwise to draw too many conclusions regarding electronic interactions based on the values obtained. They said that the norbornyl skeletons of some of the structures were clearly badly disordered, with extremely large ellipsoids and distorted geometries, while in others the ellipsoids were good, but there were high differences in the electron density peaks for the ring carbons, which strongly suggested the presence of static disorder in the crystals. Other workers in the past had also encountered disorder problems in norbornyl systems[121] so in retrospect the difficulties encountered should not have been too surprising. That the problems existed was realised early on, and the decision was made to terminate the investigation before it was complete.

4.3 Disorder in Crystals.

The determination of the structure of a molecule based on the diffraction pattern of X-rays passing through a crystal of the compound is now a much simpler task than it once was, because a number of sophisticated computer programs are commercially available to assist in this. However these heavily rely on the quality of the crystal used. A perfect crystal that diffracts strongly will give a set of data that is easy to process and refine, and establishes the position of atoms within it with a high degree of accuracy. Unfortunately such crystals are not common, and even when one is used, and a good data set is obtained, there is still some uncertainty as the positions of the atoms because of thermal motion of these within it. This problem is now usually minimised by collecting the data at low temperatures. However there are other sources of uncertainties in atomic positions that often occur. The main ones are due to *disorder* within the crystal. A perfect diffraction pattern would require that the atoms occupy the same position in every unit cell, and while there is normally a strong tendency for them to do so, variations in position do occur. The reason for this is that during the

formation of any crystal the molecules present try to occupy positions within the structure in which their energy is lowest. Mostly they manage to do so, as the other possible positions in the vicinity are normally of considerably higher energy. However sometimes they find that there are positions nearby within the unit cell that they can occupy that are of little higher energy, and some of them take these up instead. When they do so, the crystal structure is said to show some degree of disorder. The energy differences involved are usually significantly great for the majority of atoms to occupy their positions of lowest energy, so that the ability to determine the atom positions accurately is little affected. An increase in the number of these, however will lead to there being an increasing uncertainty in their true position, and this will show up as an increasing uncertainty in the calculated values of the various bond lengths and bond angles within the molecule

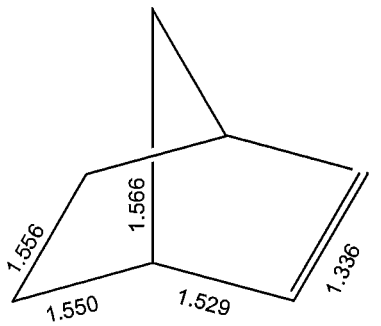
Disorder within crystals falls into two classes, *dynamic* and *static.* Dynamic disorder does not usually pose a serious problem. The thermal vibrations of molecules within the unit cell mentioned earlier is the best example of it. This is universal, and can be minimised by lowering the temperature. The other form of disorder, static disorder can be more difficult to deal with. One common example is often a problem when there are groups such as tertiary butyl or trimethylsilyl in a molecule. If these can freely rotate there are often two orientations they can take up. For example, if one of these is attached to a benzene ring, the most stable orientation would be to have one methyl above the ring and two below. However, if the two sides of the ring were distinguishable, as they could be in a crystal, the electron densities due to the methyl carbons would be spread between three positions above the ring and three positions below it. (A methyl group would show similar behaviour with regard to its hydrogens, but the positions of hydrogens in a structure are not usually determined.) In organic compounds static disorder is also found in molecules containing long flexible alkyl groups, five-membered rings, and molecules that are relatively spherical in shape. It can also be very high in biological molecules such as proteins. Sometimes it does not represent a serious problem in that it involves a part of the molecule that is of little interest, and accuracy is not a big concern. The main

problem arising from the existence of disorder is that it not only makes determining the structure more difficult, but it also makes the end product less reliable. Partly this is because it gives worse diffraction data than ordered structures, and partly because it makes refining more difficult and leads to greater uncertainties in the positions of the atoms in the crystal, and hence the bond lengths and angles.

The disorder observed in my structures was primarily due to the relatively spherical shape of the norbornyl system, which meant that slightly different orientations of it within the crystal involved relatively small changes in energy. Unfortunately this was the part of the molecule in which I was most concerned. I was advised that for C-O bond lengths of sufficient reliabilty for differences between them to be useful in my study standard deviations of the order of 0.002-0.003 would be necessary. In general these were not achieved

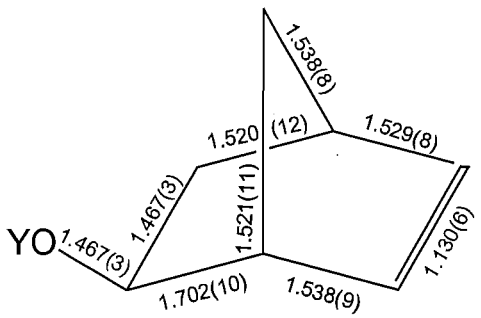
The original intent of the study had been to compare the bond lengths of the C-O in a number of exo/endo pairs in which leaving groups of differing polarities were used. However problems were encountered in the synthesis and purification of some of the derivatives, so that of the nine compounds finally studied only six consisted of exo/endo pairs. Some comments on the measured bond distances in the individual structures follow.

The best basis for comparison purposes would have been the parent alcohol 5-norbornen-2-ol.Unfortunately no structural study on this compound has been carried out. However an determination of the bond lengths in 2-norbornene has been made using a combination of electron diffraction and microwave spectroscopy[122]. The calculated bond lengths of the various C-C bonds are shown below. It is unlikely that the corresponding ones in *exo* or *endo* 5-norbornen-2-ol would be much different from these.

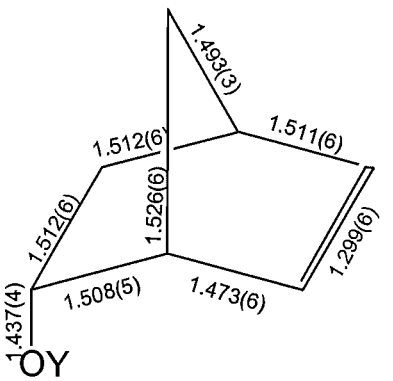


2-norbornene

The *exo/endo* pair below are for the 4-nitrobenzoate esters of the two alcohols:

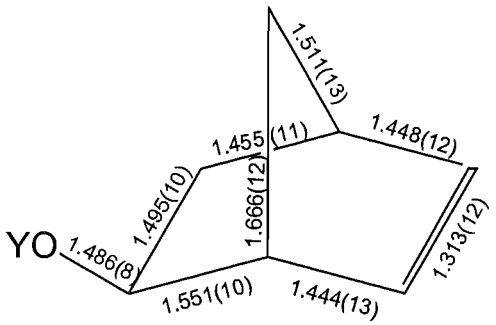


YO = *exo*-4-nitrobenzoate

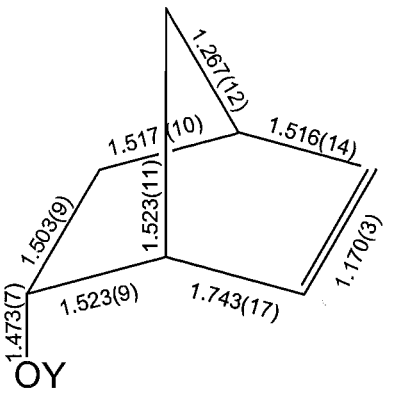


YO = *endo*-4-nitrobenzoate

The C=C bond at 1.130 Å for the *exo* 4-nitrobenzoate is clearly far too short for a bond of this type. The value for 2-norbornene of 1.336 Å is a much more realistic one for a bond of this type. While the standard deviation of the C5-O bond length would normally be acceptable, when taken in conjunction with the abnormally long C4-C5 one the determined value of 1.467 Å must be treated with considerable caution. The *endo* isomer bond lengths are a little more acceptable, but the standard deviations are on the high side, and the fact that the *exo* C-O bond appears longer than that of the corresponding *endo* isomer, while consistent with an interaction of the π system with this bond in the *exo* case occurring does not prove that this exists.

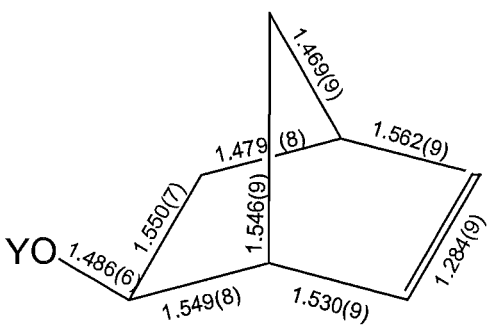


YO = *exo*-3,5-dinitrobenzoate

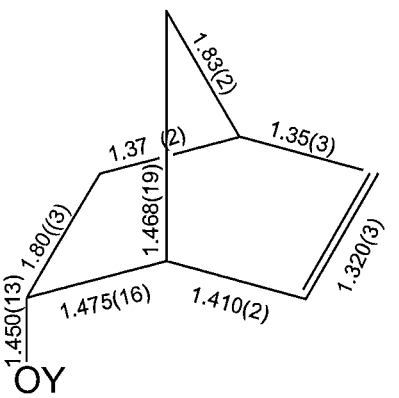


YO = *endo*-3,5-dinitrobenzoate

In the *exo*-3,5-dinitrobenzoates in the diagram above the standard deviations are really far too high for the bond lengths to be trusted. Once again (this time in the *endo* isomer) the C=C bond is unrealistically short, and it may also be noted that the C1-C7 bond iappears to be considerably shorter than even a C=C one. This is unfortunate as the 3,5-dinitrobenzoate ester is the only one for which we have reliable data in the literature with which we can compare the C-O bond length. Spiniello and White[123] have determined this in the 3,5-dinitrobenzoate ester of *cis*-1-t-butyl-4-cyclohexanol, also by X-ray diffraction and have obtained a value for this of 1.471Å with a standard deviation of 0.002. This value is considerably shorter than that obtained for my *exo* isomer, but comparable in length with my *endo* one, once again, consistent with my values but not confirming that they can be relied on.



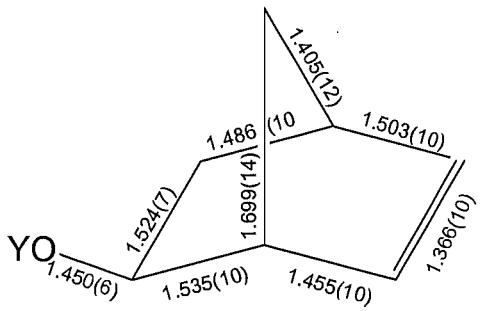
YO =*exo*-4-bromobenzenesulfonate



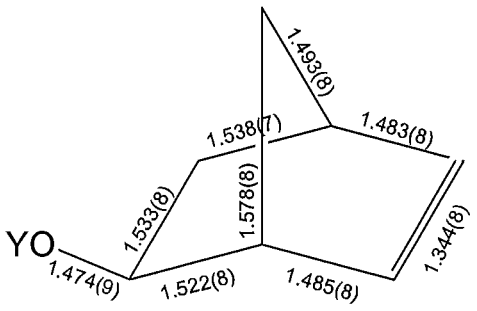
YO = *endo*-4-bromobenzensulfonate

The last exo/endo pair that was investigated was the the 4-bromobenzenesulfonates. The *exo* isomer suffers from the same problem as that for the previous pair – unacceptably high values for the standard deviations. Once again the C-O bond length is longer than that in the *endo* isomer, as it should be if the π bond was interacting with the C-O bonding orbital. However this observation must be treated with extreme caution in view of the extremely high standards deviations obtained for the *endo* isomer for not only C5-O, but also both the C5-C4 and C5-C6 bonds.

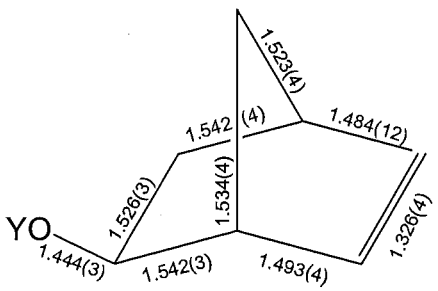
Lastly, there are three compounds that were studied, but for which only one isomer was available.



OY = *exo*-3-nitrobenzoate



OY = *exo*-3-nitrobenzenesulfonate



OY = *exo*-4-nitrophenoxy

The difficulty in commenting on these results is that, even setting aside the problem of bond length uncertainties, we do not have the other isomers to compare them with. The C5-O distance in the first, the *exo*-3-nitrobenzoate, may

be compared with those for the corresponding *exo*-4-nitrobenzoate and *exo*-3,5-dinitrobenzoate. The C5-O bond lengths found for these were 1.467(3) Å and 1.486(8) Å respectively. The order for the three (3-nitro < 4-nitro < 3,5-dinitro) parallels that for the expected stabilities of the three benzoate ions. In the *endo* series, the lengths of the C5-O bonds follow the same order (4-nitro < 3,5-dinitro) and it was also found that the C5-O distances were in both cases longerfor the *exo* derivatives than the *endo* ones. The consistency observed in these results tends to give one more confidence in them than can be gained from the standard deviations in the calculated bond lengths.

If one applies the same approach to the second compound, the *exo*-3-nitrobenzenesulfonate, then one should be able to compare the C5-O bond length with those for the *exo*- and *endo*-4-bromobenzenesulfonates. We would expect the C5-O distance for the *exo*-3-nitro compound (1.474(9) Å) to be greater than that for the *exo*-4-bromobenzenesulfonate. However the C-O bond in the latter , at 1.486(6) Å is the longer of the two. However the difference is not great, and in this case the high standard deviations may account for this.

The last compound, the *exo*-4-nitrophenyl ether, lacked an *endo* counterpart because this could not be synthesised. The method used, the reaction of the sodium salt of the *endo* norbornenol with 4-fluoronitrobenzene gave only the *exo* ether. The reaction required the used of very strongly basic conditions (NaH/THF) and it is likely that epimerisation of either the alcohol or the product occurred. The 4-nitrophenoxy group is a much poorer leaving group than any of the others used, and the C5-O bond length should therefore be shorter than those of all of the other compounds studied. The determined value of 1.444 (3) Å is consistent with this.

4.4 Summary

The high observed standard deviations in the bond lengths are consistent with the existence of static disorder within the crystal. In many cases the C-C and

C=C bond lengths differ substantially from those expected, based on those present in 2-norbornene itself. On the other hand, the observed differences in the C-O bond lengths are consistent with the leaving abilities of the various groups attached to the C5. Such differences cannot be taken as indicating interaction between the C-O bonding orbitals and the π system of the C2 - C3 bond, as they would be predicted, even if none existed. Establishing this requires that the C-O bond lengths be consistently shorter in the *endo* isomers than in the corresponding *exo* ones. In the three cases where these could be compared, this was in fact observed. However if one bears in mind the uncertainties involved in the atomic positions, unless supported by other evidence one cannot conclude that the existence of the interaction in 5-exo-substituted alkenes as having been established.

Chapter 5.

EXPERIMENTAL PART 1: Preparation of Norbornenes

5.1 INSTRUMENTATION AND REAGENTS

All of the 5-substituted-2-norbornenes prepared were known compounds and were made by the methods used for these or modifications of them. Unfortunately almost all are liquids at room temperatures, making comparison of the products obtained with those obtained by others a problem, since melting points could not be used. It was decided that the best way of confirming the identity and purity of the compound obtained was by analysis of their ^{1}H and ^{13}C nuclear magnetic resonance spectra, using standard techniques. It was considered that identifying the product and establishing its purity by this means was superior to comparison of its properties with ones listed in the literature, especially since most of the preparations pre-dated the widespread use of high field NMR.

^{1}H NMR spectra were recorded on a Varian Unity 500 MHz instrument fitted with a 3 mm probe and are referenced to the Me_4Si signal for $CDCl_3$ solutions. ^{13}C NMR spectra were recorded on a Varian Unity 300 MHz instrument, operating at 75 MHz, with a delay (D1) of 1s using a 3 mm probe in $CDCl_3$ and are referenced to the internal Me_4Si solvent signal. All spectra were recorded at 23°C. All other one dimensional, ^{1}H nOe, 1-D NOESY and two dimensional, COSY, GHSQC, GHMBC) NMR experiments were carried out on a Varian Unity 500 using standard pulse sequences and parameters. Unless otherwise stated the values for chemical shifts (measured in parts per million, ppm) are assigned to the average of the multiplets.

Chromatographic separation of samples was carried out using HPLC columns or normal glass columns for column chromatography. For HPLC the solvent used was HPLC grade acetonitrile and milli-Q water. Analytical HPLC was performed on a Shimadzu LC-10AD VP liquid chromatograph coupled to SIL-10A VP auto injector, a CTO-10AVP column oven at 40 °C and detecting with

a photo diode array detector. Preparative HPLC was carried on a column C18 83–221-C. Column chromatography performed with silica gel (grade 923, 100-200 mesh). The solvents used were commercial solvents purified and dried according to standard methods[124]. Unless otherwise stated 'petroleum ether' refers to the fraction boiling between 50°-70°C and 'ether' to diethyl ether.

The coupling of chromatographic separation of products with identification by means of NMR techniques permitted the alkenes to be prepared, purified, and identified on a much smaller scale than many of the preparations previously used in the literature. This was particularly convenient, since only small amounts of material were required for the investigations.

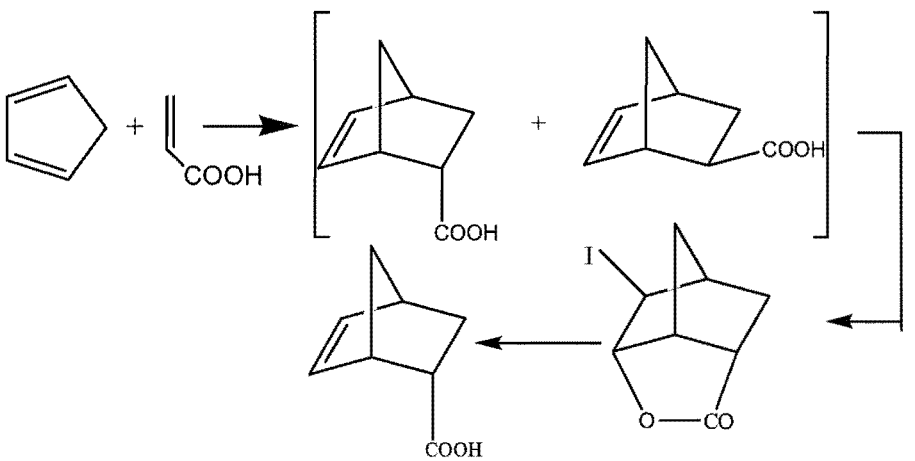
Infrared and Mass spectra were occasionally used in the course of the work, from time to time. Infrared spectra were recorded on either a Perkin Elmer 1600 FTIR or Shimadzu 8201PC series FTIR spectrophotometer interfaced with Shimadzu's HyperIR software,. Measurements were made by absorption or reflection after mixing (grinding) samples with potassium bromide crystals. Mass spectra were obtained by means of a Kratos MS80RFA spectrometer with a Mac 3 data system.

5.2 PREPARATION OF 5-SUBSTITUTED-2-NORBORNENES

PROCEDURES

5.2(i). *Preparation of 5-exo and 5-endo-2-norbornene carboxylic acids*[125-7]

The two acids, which were also used for the preparation of the cyano- and acetyl derivatives were prepared by the reaction between cyclopentadiene and acrylic acid in cyclohexane.[125] Small samples of the pure *endo* and *exo* acids could be obtained from the crude product by column chromatography, but this method was not suitable for larger amounts of material. Instead the mixture of acids obtained was separated into its components by conversion of the *endo* form into an iodolactone, extracting the *exo*-form with base, and regenerating the *endo*- form by treating the lactone with zinc and acetic acid[126,127].



(5.2.1)

a) Preparation of the *endo/exo* acid mixture[125]

Freshly distilled cyclopentadiene (16.5 g, 0.25 mol) was mixed with acrylic acid (15 g, 0.20 mol) at room temperature. The solution grew hot and after 30 minutes started to boil. It was allowed to stand for 4 hours at room temperature and then poured into water and the solution made alkaline with 2M NaOH. The whole mixture was then shaken with ether (100 mL ×3) to remove

any unreacted alkene, the aqueous layer acidified with 2M HCl, and the acid showed the ratio of *exo* to *endo* acid was 27:73.

b) Preparation of the iodo lactone.[126,127]

A portion of the *exo/endo* acid mixture (10 g, 0.072 mol) was neutralised with 10% NaOH and then 300 mL of 0.25M sodium carbonate solution was added. This basic solution was mixed with iodine (17 g, 0.13 mol), dissolved in a solution of 42 g, (0.25 mol) of potassium iodide in 300 mL of water. The solution was stirred well for 24 hours in the dark (which separated as a dark oil) was extracted with dichloromethane. The dichloromethane layer washed with water and dried over $MgSO_4$. Evaporation of the dichloromethane under reduced pressure gave 18 g of crude product. A dark precipitate formed. This was extracted with ether, (100 mL × 3). The aqueous phase contained the *exo* acid as the sodium salt and was set aside. The ether layer was washed with 10% $Na_2S_2O_3$ until colourless, dried over $MgSO_4$ and evaporated under reduced pressure. The iodo lactone was obtained as a yellow oil. Yield: 9.9 g (73%).

c) Preparation of the *endo* acid

The yellow oil was mixed with 50 mL of acetic acid and 1 0 g of zinc dust and stirred at 15°C for 3 hours and at room temperature for a further 2 hours. The solution was then filtered and the precipitate of zinc residues washed with acetic acid followed by ether. The filtrate was mixed with water, extracted with ether, and the ether layer washed with water and dried over anhydrous $MgSO_4$. Removal of the ether by vacuum evaporation gave an oil. Any acetic acid present was removed under reduced pressure and the residue recrystallised from pentane. White crystals of the pure *endo* acid (m.p. 44°) were obtained. The yield was 5.13 g (71% of theory).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.91 (s, 1H, H1), 6.20 (dd, 1H, J = 3.2, 5.5 Hz, H2), 5.99 (dd, 1H, J = 2.8, 5.5 Hz, H3), 3.23 (s, 1H, H4), 2.99 (dt, 1H, J = 3.9, 7.9, 9.1 Hz, H5x), 1.91 (m, 1H, J = 2.4, 3.9, 5.2, Hz, H6x), 1.39 (m,1H, J = 1.4, 2.7, 4.2, Hz, H6n), 1.44 (m, 1H, H7a), 1.29 (d, 1H, J = 8.3 H7s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 42.49 (C1), 137.86 (C2), 132.40 (C3), 45.64 (C4), 43.24 (C5), 29.04 (C6), 49.66 (C7), 181.36 (C8).

d) Separation of the *exo* acid

The basic solution from (b) contained the *exo* acid in the form of its sodium salt. This was treated with just sufficient 10% $Na_2S_2O_3$ solution to remove any iodine and then acidified with dilute HCl. The *exo* acid precipitated and was extracted with ether (30 mL × 3). The extract was washed with water and 1% $Na_2S_2O_3$ solution, dried over $MgSO_4$ and the solvent removed under reduced pressure. The yield obtained was 2.05 g (76%).

^1H NMR (500 MHz $CDCl_3$) δ 2.94 (s, 1H, H1), 6.16 (t,1H, J = 2.9, 5.9 Hz, H2), 6.12 (t, 1H, J = 2.9, 5.3 Hz, H3), 3.11 (d, 1H, J = 1.5 Hz, H4), 2.27 (m,1H J = 1.9, 4.4, 5.9, 8.8, Hz, H5n), 1.96 (dt, 1H, J = 3.9, 4.4, 8.3, 11.2, Hz, H6x), 1.41 (m, 1H, J = 2.4, 8.8, 11.2, Hz, H6n), 1.54 (d,1H, J = 8.3 Hz H7s), 1.38 (t,1H, J = 1.4, Hz, H7a) .

^{13}C NMR (75 MHz, $CDCl_3$) δ 41.64 (C1), 138.12 (C2), 135.69 (C3), 46.9 (C4), 43.42 (C5), 30.3 (C6), 46.37 (C7), 182.81 (C8).

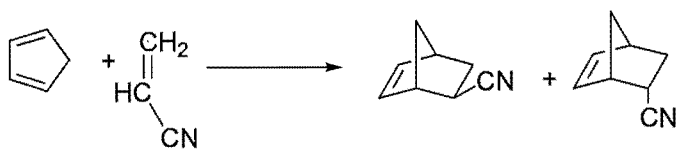
e) Separation of the *exo* and *endo* acids by column chromatography.

Approximately 0.5 g of the *exo/endo* acid mixture was dissolved in a small quantity of 90:10 petroleum ether:ethyl acetate. The solution was poured on to 5 g of dry silica in a 30cm column, and eluted with 90:10 petroleum ether:ethyl acetate. The first fraction to come off the column was the pure *exo* acid, (95 mg, 70% recovery). This was followed by 125 mg of a mixed fraction. The third and last fraction consisted of the pure *endo* acid, (250 mg, 70% recovery). The ^1H and ^{13}C NMR spectra of the *exo* and *endo* acid samples obtained from the chromatographic separation and the iodo lactone methods were found to be identical. The chromatographic method is the simpler of the two, but less suited to large scale separations. It was therefore only used when small amounts of the two acids were needed.

5.2(ii) Preparation of 5-*exo*- and 5-*endo*-cyanonorbornenes

Two methods were used to prepare the above compounds. The first (Method A) was by the Diels-Alder addition of cyclopentadiene to acrylonitrile. This gives a mixture of the *exo* and *endo* adducts in approximately equal amounts. These were subsequently separated by column chromatography. The second (Method B) avoided the separation stage by preparing the two nitriles from the corresponding carboxylic acids. In a one-pot synthesis these were reacted with ammonia and ethyl polyphosphate. While this method had the disadvantage of requiring the prior preparation of pure samples of the two acids, these were available on a large scale by the iodo lactone method.

Method A[128,129]



(5.2.2)

Freshly distilled cyclopentadiene (8.25 g, 0.12 mol) was added to 100 mL of ether in a 250 mL round-bottomed flask. To this was added 6.25 g,(0.12 mol) of acrylonitrile and and the mixture was stirred at room temperature for 24 hours. The ether was removed under reduced pressure. The crude product was purified by silica column chromatography. Any unreacted cyclopentadiene (or dicyclopentadiene) present was removed by initial elution with petroleum ether. Subsequent elution with 90:10, petroleum ether:ethyl acetate gave 8.3 g (55% yield) of a mixture of the two isomeric 5-cyano-norbornenes

^{1}H NMR analysis of the mixture[130] showed that the ratio of *exo* to *endo* isomers was 56: 44, a figure similar to that in the literature.

A sample of the 5-*exo*- and 5-*endo*-cyano-2-norbornene mixture (100 mg) was dissolved in 1 mL of 90:10 petroleum ether:ethyl acetate, poured on to a dry silica column (ratio 1:100) and eluted with the same solvent mixture. A low pressure was applied to the column. The retention time of pure 5-*exo*-cyano-2-norbornene was lower than that of the 5-*endo*-cyano and accordingly eluted first. The yield of pure *exo* isomer was 35 mg. This was followed by a small amount of a mixed fraction (about 20 mg). Finally the pure 5-*endo*-cyano-2-norbornene came off. About 40 mg of this was obtained.

5-*exo*-cyano-2-norbornene

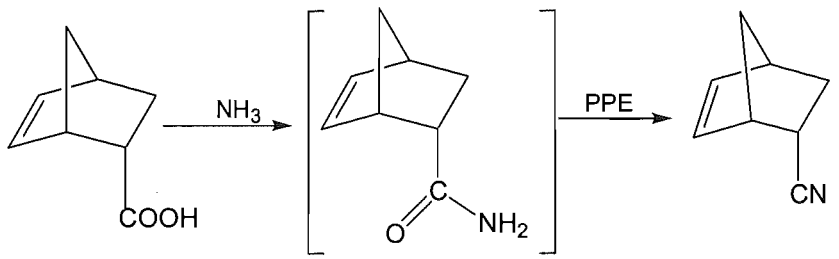
^{1}H NMR (500 MHz, $CDCl_3$) δ 3.03 (s , 1H, H1), 6.33 (dd, 1H, J =2.9. 5.9 Hz, H2), 6.19 (dd, 1H, J = 2.9, 5.9 Hz, H3), 3.23, (s, 1H, H4), 2.86 (dt, 1H, J = 3.9, 7.8, 9.3 Hz , H5x), 2.14 (m, 1H, H6x), 1.32 (dt, 1H J = 2.9, 4.9, 3.9, 11.7 Hz, H6n), 1.51 (td, 1H J = 2.0, 2.4, 4.4, Hz, H7a)1.20 (d, 1H, J = 8.8 Hz, H7s).
^{13}C NMR *endo*- (75 MHz, $CDCl_3$) δ 42.25 (C1), 138.74 (C2), 132.61 (C3), 48.4 (C4), 27.07 (C5), 32.35 (C6), 45.62 (C7), 123.00 (C8).

5-*endo*-cyano-2-norbornene

^{1}H NMR ^{1}H NMR (500 MHz, $CDCl_3$), δ 3.05 (s, 1H, H1), 6.17 (t, 1H, J = 2.9, 5.9 Hz, H2), 6.04 (t, 1H, J = 2.9, 5.9 Hz, H3), 3.23 (d, 1H, J = 1.5 Hz, H4), 2.18 (tt, 1H, J = 2.0, 1.5, 4.9 Hz, H5n), 1.97 (m, 1H, J = 3.9, 4.4, 12.3 Hz, H6x), 1.58 (d, 1H, J = 1.5 Hz, H6n), 1.56-1.54 (m, 2H, J = 1.5, 8.8 Hz, H7a, H7s).
^{13}C NMR (75 MHz, $CDCl_3$) δ 41.75 (C1), 138.06 (C2), 133.96 (C3), 47.36(C4), 27.13 (C5), 32.12 (C6), 47.09 (C7), 123.55 (C8).

Method B

5-endo cyano-2-norbornene



(5.2.3)

Preparation of polyphosphate ester(PPE) [131]

Phosphorus pentoxide (15 g, 0.1 mol) was added to 30 mL of anhydrous ether and 15 mL of dry chloroform. This mixture was refluxed for 4 days. The excess solvent was then removed under reduced pressure, to leave a colourless viscous liquid in 100% yield. This was pure enough to be used for preparing the cyano derivative below.

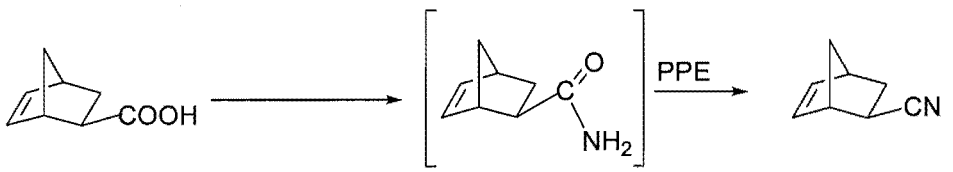
Preparation of 5-endo-cyano-2-norbornene[132]

2-Norbornene-5-*endo*-carboxylic acid (500 mg, 3.6 mmol) was placed in a 100 mL two-necked R.B. flask and dissolved in 2 mL of dry chloroform. This was mixed with 2 g of freshly prepared polyphosphate ester (PPE) and stirred under anhydrous ammonia gas in an ice-salt bath at -5 °C for 30 minutes. This mixture was then allowed to warm up to room temperature and stirring was continued for 1.5 hours. After this time another 3 g of PPE was added and the treatment with ammonia stopped. The resulting viscous mixture was heated on a water bath at 80^0C for 6 hours. After the mixture had cooled, 20 mL of 25% sodium carbonate solution was added with stirring. The *endo* cyano product formed was extracted with ether (20 mL ×3). The ether layer was then dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum gave 320 mg (74%) of

5-*endo*-cyano-2-norbornene. This was sufficiently pure to be used for further reactions without further purification.

^{1}H NMR (500 MHz, $CDCl_3$),δ 3.02 (s,1H, H1), 6.33 (dd, 1H, J=2.9. 5.9 Hz, H2), 6.19 (dd,1H, J = 2.9, 5.9 Hz, H3), 3.23 (s, 1H, H4), 2.86 (dt, 1H, J = 3.9, 7.8, 9.3 Hz, H5x), 2.14 (m,1H, H6x), 1.51 (td, 1H, J = 2.0, 2.4, 4.4, Hz, H7a) 1.32 (dt, 1H 1, J = 2.9, 3.9, 4.9, 11.7 Hz, H6n), 1.20 (d, 1H, J=8.8 Hz, H7s).
^{13}C NMR *endo*- (75 MHz, $CDCl_3$) δ 42.25 (C1), 138.74 (C2), 132.61 (C3), 48.4 (C4), 27.07 (C5), 32.35 (C6), 45.62 (C7), 123.00 (C8).

5-*exo*-cyano-2-norbornene



(5.2.4)

2-Norbornene-5-*exo*-carboxylic acid (350 mg, 2.5 mmol) was mixed with 2 mL of dry chloroform and 2 g of polyphosphate ester (PPE) in a two necked 100 mL R.B flask. It was then stirred under anhydrous ammonia gas in an ice bath at –5°C for 30 minutes.[132] A further 3 g of PPE was added, the ice bath removed, and stirring under ammonia was continued for 1.5 hours at room temperature. At this point the treatment with NH_3 gas was discontinued, a further 3 g of PPE added, and the mixture heated on a water bath at 80 °C for 6 hours. After cooling, the mixture was shaken with 50 mL of 25% Na_2CO_3 solution and then the cyano compound taken up in ether (3 x 30 mL). The combined ether extracts were dried over anhydrous Na_2SO_4 and the ether evaporated. About 355 mg of coloured material was obtained. This was purified by passing through a short silica column using ether as eluent to give the pure 5-*exo*-2-cyanonorbornene. The yield was 257 mg (85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.05 (s, 1H, H1), 6.04 (dd, 1H J = 2.9, 5.9 Hz, H2) 6.16 (dd, 1H , J = 2.9, 5.4 Hz, H3), 3.23 (d, 1H, J = 1.5 Hz, H4), 2.18 (m,1H,

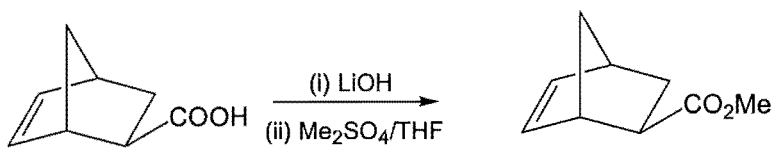
J = 1.5, 1.9, 4.9, 9.8 Hz, H5n), 1.97 (dt, 1H, J = 3.9, 4.4, 7.8, 12.2 Hz, H6x), 1.58 –1.54 (b, 3 H, H6n, H7a, H7s)

^{13}C NMR (75 MHz, $CDCl_3$) δ 41.75 (C1), 133.96 (C2), 138.06 (C3), 47.36 (C4), 27.13 (C5), 32.12 (C6), 47.09 (C7), 123.55 (C8).

5.2(iii) Preparation of 5-*exo*-and 5-*endo*-methoxycarbonyl-2-norbornenes

An *endo*/*exo* mixture of these could be prepared without difficulty from cyclopentadiene and methyl acrylate, but initial attempts to separate the two esters by chromatography were unsuccessful. However this problem was eventually overcome. Because of this problem a second method was adopted in which they were prepared from the corresponding acids. In order to avoid the possibility of epimerisation of the carboxyl group or protonation of the double bond that might lead to skeletal rearrangement, conversion to the esters was carried out by alkylation of their lithium salts with dimethyl sulfate[133]. The workup procedure used differed slightly from that mentioned in the literature.
Both methods are given below.

a) 5-exo-methoxycarbonyl-2-norbornene.



(5.2.5)

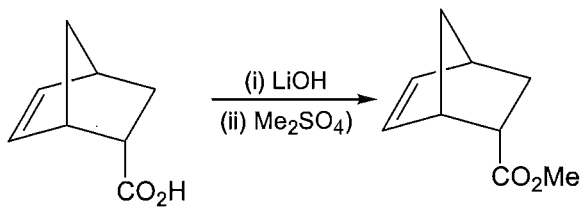
5-Norbornene-2-*exo*-carboxylic acid (345 mg, 2.5 mmol), was dissolved in 2.5 mL of dry THF, and stirred with $LiOH.H_2O$ (110 mg, 2.5 mmol), at room temperature for 30 minutes. To this 0.24 mL of dimethyl sulphate was added and the solution refluxed on a water bath for 5 hours. The condenser was then washed with a little ether and removed from the flask and the heating continued until all of the ether and THF had been driven off (approximately 10 minutes). The residue was then shaken with 25 mL of saturated $NaHCO_3$ solution and the ester was

extracted with ether (20 mL × 3). The extracts were dried over anhydrous $MgSO_4$, and the ether evaporated. The yield of *exo* ester was 0.290 mg (75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.92 (s, 1H, H1), 6.14 (dd, 1H J = 2.9, 5.4 Hz, H2), 6.10 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.04 (d, 1H, J = 1.0 hz, H4), 2.28 (m, 1H, H5n), 1.92 (dt, 1H J = 3.9, 3.4, 7.8, 11.7 Hz, H6n), 2.23 (dd, 1H J = 4.4, 4.9, 9.3 Hz, H6x), 1.38 (m, 1H J = 1.5,2.9,9.3 Hz, H7a), 1.53 (d, 1H J = 8.3 Hz, H7a), 3.69 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$) δ 46.55 (C1), 138.04 (C2), 135.72 (C3), 42.96 (C4), 41.61 (C5), 30.32 (C6), 46.34 (C7), 176.74 (CO), 51.70 (OCH_3)

b) *5-endo-methoxycarbonyl-2-norbornene*



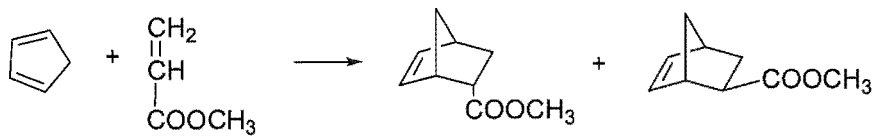
(5.2.6)

5-Norbornene-2-*endo*-carboxylic acid (345 mg 2.5 mmol) in dry THF (2.5 mL) was stirred with $LiOH.H_2O$ 109.5 mg (2.5 mmol) at room temperature for 30 minutes. To this 0.24 mL (2.5 mmol), of freshly distilled dimethyl sulfate was added and the solution was refluxed on a water bath at 70°C for 5 hours[133]. The THF then removed by distillation using a hot water bath, the residue extracted with ether (3 x 15 mL), washed with $NaHCO_3$ solution, and water and the ether layer dried over anhydrous $MgSO_4$. Evaporation of the ether gave 217 mg of the *endo* ester (63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.90 (s, 1H, H1), 6.17 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.91 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.20 (s, 1H, H4), 2.94 (dt, 1H J = 3.6, 4.0, 7.9, 9.1 Hz, H5x), 1.39 (m, 1H H6n), 1.90 (m, 1H J = 3.2, 3.9, 5.9, 9.1 Hz H6x), 1.42 (dd, 1H J = 3.2, 5.9 Hz, H7a), 1.27 (d, 1H J = 8.7 Hz, H7a), 3.62 (s, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$), δ 42.45 (C1), 137.66 (C2), 132.29 (C3), 45.56 (C4), 43.09 (C5), 29.18 (C6), 49.54 (C7), 175.15 (CO), 51.39 (OCH_3).

5.2(iv) Diels-Alder preparation of 5-*exo*- and 5-*endo*-methoxycarbonyl-2-norbornenes



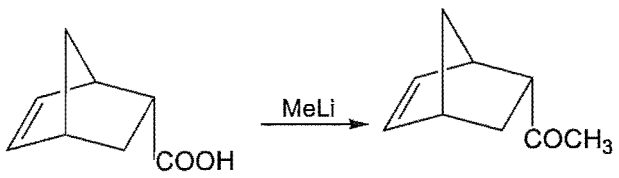
(5.2.7)

Freshly distilled cyclopentadiene (8.5 g, 0.128 mol) was added to 100 mL of anhydrous ether. To this 11 g, (0.127 mol) of methyl acrylate was added and the solution was stirred at 40 °C for 15 minutes. The mixture was then stoppered and kept overnight. The solvent was removed by rotary vacuum evaporation. The crude product was passed through a silica column using petroleum ether as eluent in order to remove any unreacted olefin. The *exo/endo* mixture of 5-carbomethoxy-2-norbornenes was then stripped off the column with ether. The yield was 9.62 g (59%). The *exo*: *endo* ration was determined by NMR to be 25:75

The *exo/endo* mixture of esters was separated on a dry silica column. Approximately 200 mg of the mixture was dissolved in a small amount of 80:20 petroleum ether:ether, poured over a dry silica column (1 0 g of silica) and eluted with the same solvent mixture. The first fraction eluted was 5-*exo*-carbomethoxy-2-norbornene. The amount obtained was 60 mg (30%). This was followed by 20 mg of mixed esters, and lastly 120 mg of pure 5-*endo* product (60%) [134]. The NMR data of both were identical to the esters prepared from the corresponding acids.

5.2(v) Preparation of 5-*endo*-acetyl-2-norbornene.

This was prepared according to the literature procedure by the reaction of methyllithium with the *endo* carboxylic acid. [135,136]



(5.2.8)

2-Norbornene-5-*endo*-carboxylic acid (300 mg, 2.2 mmol) was dissolved in 18 mL of anhydrous THF under nitrogen and it was then cooled in ice bath containing a small amount of $CaCl_2$. This solution was vigorously stirred and 6.6 mmol (14.4 mL of 0.6 molar) methyllithium in ether) was added. Stirring was continued at this temperature for three hours. After this time, 7 mL of chlorotrimethylsilane was added and after stirring for 2 minutes, 15 mL of 1M HCl. Stirring was continued for a further 30 minutes at room temperature. The ether layer was separated and the aqueous layer extracted twice with 25 mL of ether. The ether extracts were mixed, washed with water, (50 mL x 3) and then dried over anhydrous $MgSO_4$ Evaporation of the solvent gave 280 mg of the *endo* ketone.

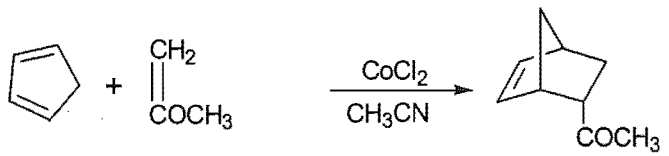
This was further purified by chromatography on silica. The eluent used was 1:1 ether:petroleum ether. The second fraction to come off the column was pure *endo*-5-acetyl-2-norbornene. Yield = 253 mg, 85%.

^{1}HNMR (500 MHz, $CDCl_3$) δ 2.90 (s, 1H, H1), 6.15 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.86 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.24 (d, 1H J = 9.3 Hz, H4), 3.01 (dt, 1H J = 3.4, 3.9, 4.9, 7.8 Hz, H5x), 1.49 (t, 1H J = 2.4, 3.9, Hz, H6n), 1.75 (m, 1H J= 2.9, 3.9, 4.9, 9.3 Hz, H6x), 1.46 (m, 1H J = 2.0, 2.9, 4.4, 11.2 Hz, H7a), 1.34 (t, 1H J = 8.3, 9,3 Hz, H7s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 42.47 (C1), 137.62 (C2), 131.02 (C3), 45.64 (C4), 52.11 (C5), 27.19 (C6), 49.74 (C7), 208.68 (CO), 28.98 (CH_3).

5.2(vi) Alternative method for preparing the *endo* isomer

It was subsequently found that the *endo* ketone could be obtained by the Diels-Alder route if the reaction was carried out in acetonitrile in the presence of cobaltous chloride[137]:



(5.2.9)

In a two necked 100 mL R.B. flask 1.5 g (0.23 mol) of freshly cracked cyclopentadiene and 500 mg cobaltous chloride were dissolved in 15 mL of dry acetonitrile. This was followed by 1.44 g (0.02 mol) of freshly distilled methyl vinyl ketone. The solution was stirred under nitrogen for 14 hours, and the acetonitrile was then removed by means of a rotary evaporator. The residue was then shaken with ether (15 mL × 3) and ether extract dried over anhydrous $MgSO_4$. The ether was then evaporated to give 1.46 g of product. This was further purified by passing through a silica column, eluting with 7:3 petroleum ether:ether. The first fraction to elute was unreacted cyclopentadiene. The second was pure 5-*endo*-acetyl-2-norbornene. The yield was 850 mg (31%) and the ^1H NMR did not show even traces of *exo* isomer. The yield was not high, but no attempt was made to optimise the reaction conditions.

5.2(vii) Preparation of 5-*exo*-acetyl-2-norbornene

This compound was also prepared by two routes. The first, from the *exo* acid is the same as the one used for the corresponding *endo* isomer.

Method A[135,136]

(5.2.10)

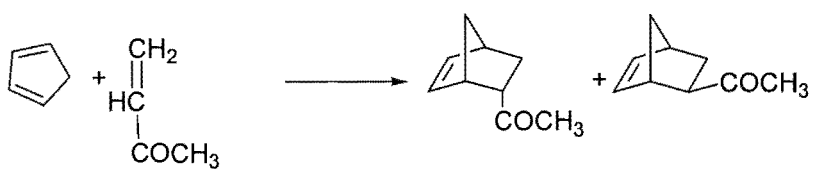
2-Norbornene-5-*exo*-carboxylic acid (300 mg, (2.2 mmol) was dissolved in 15 mL of anhydrous THF under nitrogen. The solution was cooled in an ice/$CaCl_2$ bath, 15 mL of 0.6M methylithium in ether added, and the whole stirred at this temperature for 3 hours. Chlorotrimethylsilane (7 mL) was added and the solution stirred for two minutes to destroy any excess methyllithium. The mixture was brought to room temperature; 15 mL of 1M HCl added, and the solution stirred for 30 minutes. The organic layer was separated and the aqueous layer extracted three times with 20 mL portions of ether. The ether layers were combined, washed twice with 50 mL of water, dried over anhydrous $MgSO_4$ and the ether evaporated. The yield of crude *exo* ketone obtained was 240 mg (81%). This was further purified by silica column chromatography using petroleum ether:ether in 1:1 ratio as eluent. The NMR was not sufficiently resolved to calculate coupling constants. Those obtained from the product obtained by Method B are given below (**5.2.11**).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.89 (s, 1H, H1), 6.15 (dd, 1H, J = 2.9, 5.4 Hz, H2), 6.12 (t, 1H, J = 2.0, 5.4 Hz,H3), 2.99 (s, H4), 2.38 (dd, 1H, J = 4.4, 4.9 Hz, H5n), 1.27 (d, 1H, J = 9.3 Hz H6n), 1.88 (m, 1H, H6x), 1.32 (s, 1H, H7a), 1.29 (s, 1H, H7s).2.20 (d, 3H, J = 1.9 Hz, CH_3)

^{13}C NMR (75 MHz, $CDCl_3$) 41.66 (C1), 138.23 (C2), 135.78 (C3), 45.34 (C4), 51.68 (C5), 29.02 (C6), 45.93 (C7), 210.73 (CO), 29.84 (CH_3)

Method B

The Diels-Alder addition of cyclopentadiene to methyl vinyl ketone under normal conditions gave a mixture of *exo* and *endo* products.



(5.2.11)

This isomeric mixture could be separated into its individual components by chromatography on silica using 9:1 petroleum ether:ether, 9:1 as eluent. The first

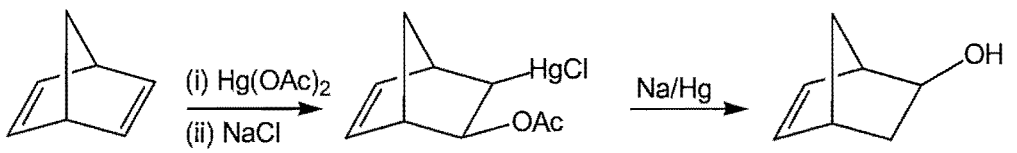
fraction to appear was the pure 5-*exo*-acetyl-2-norbornene, This was followed by a small amount of mixed fraction and finally the pure 5-*endo*-acetyl-2-norbornene.

5.2(viii) Preparation of 5-*exo*- and 5-*endo*-hydroxy-2-norbornenes

The Diels-Alder method could not be used for the synthesis of the *exo*- and *endo*-5-hydroxy-2-norbornenes as the dienophile (ketene) does not react with cyclopentadiene to give these products. The alternative approach of replacing the carboxyl group of the appropriate carboxylic acid by a hydroxyl group did not appear a realistic route. A survey of the literature showed that there was no method that gave a mixture of the *endo* and *exo* alcohols from which the two isomers could be obtained by chromatography. Previous preparations had all involved their independent preparation. The most common method for making the *exo* isomer involved oxymercuration-demercuration of one of the double bonds of norbornadiene, while the *endo* isomer was best obtained by the reduction of 2-norbornenone.

a) 5-*exo* Hydroxy-2-norbornene

The oxymercuration of one of the double bonds of norbornadiene followed by demercuration using sodium borohydride had been previously used for the preparation of the above 5-*exo*- alcohol[80,138,139]. However in my hands the major product of the reaction was a diol. Less than 1% of the desired alcohol was obtained. However Mayo and co-workers[81], who also encountered difficulty with this preparation, subsequently reported that isolation of the intermediate mercury derivative, followed by reduction of this using sodium amalgam gave the required compound.



(5.2.12)

To a solution of norbornadiene (5.39 mL, 50 mmol) dissolved in 25 mL of THF (freshly distilled from Na/benzophenone), was added (with stirring) 10.4 g

(32.6 mmol) of mercuric acetate over a period of 1 hour. The mixture then was stirred at room temperature for 12 hours. It was then treated with 14.6 g (25 mmol) of sodium chloride and stirring continued for 30 minutes. The mixture was then added to 200 mL of water and extracted four times with 30 mL of dichloromethane. The combined CH_2Cl_2 extracts were washed twice with brine (50 mL), separated, and dried over $MgSO_4$. Evaporation using a rotary evaporator gave 12 g of the crude product. Recrystallisation of this from ethyl acetate gave 8.2 g of the pure oxymercurial.

This material was shaken with 200 mL of 2.5M sodium hydroxide in a 500 mL round-bottomed flask. Approximately 50 g of 6% (w/w) sodium amalgam was added and the mixture stirred at room temperature. After 4 hours another 50 g of sodium amalgam and stirring continued. After 18 hours the mixture was quenched with 200 mL of water. The demercuration product formed was extracted into ether by shaking the mixture with four 200 mL aliquots. The ether layer then washed with 200 mL of brine solution and dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure gave 1.86 g of the alcohol (82%). This was further purified by passing through a silica column (1:20) using as eluent petroleum ether:ethyl acetate (80:20). The second fraction to emerge was the pure *exo* alcohol. Yield = 1.78 g (77%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.69 (s, 1H, H1), 6.15 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.93 (dd, 1H J = 2.9, 5.9 Hz, H3), 2.79 (s, 1H, H4), 3.87 (t, 1H J = 5.9, 6.8 Hz, H5n), 1.26 (m, 1H, H6n), 1.57 (m, 1H J = 2.0, 3.4, 5.9, 8.8 Hz, H7a), 1.55 (dd, 1H J = 1.5, 2.9 Hz, H7s).

^{13}C NMR (75 MHz, $CDCl_3$) δ 40.62 (C1), 140.19 (C2), 133.29 (C4), 50.08 (C5), 72.44 (C5), 45.45 (C6), 37.01 (C7).

b) 5-*endo* Hydroxy-2-norbornene.

The required starting material, 2-norbornenone, was not commercially available. Two different procedures were used for its preparation. The first method involved the Diels-Alder addition of cyclopentadiene to 1-cyanovinyl acetate, followed by hydrolysis of the adduct. The second, more direct route, was

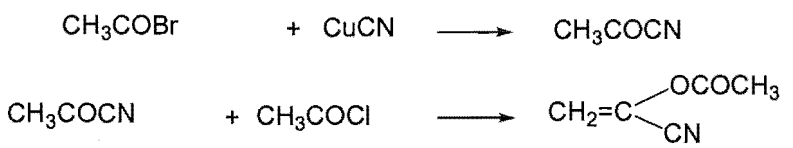
by the oxidation of commercially available 2-norbornenol. The second method was more convenient when only small quantities of material were required.

5.2(ix) Preparation of 5-Norbornen-2-one

Method A

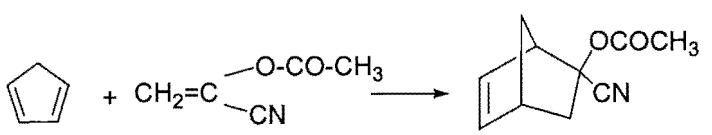
1-Cyanovinyl acetate

1-Cyanovinyl acetate is commercially available, but is expensive. However it can be easily prepared[20].



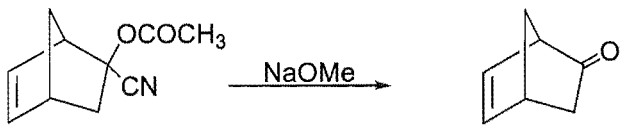
Acetyl cyanide is first prepared by the slow addition of 4.0 g of cuprous cyanide to 55 g of refluxing freshly distilled acetyl bromide. After one hour the black residue was distilled and the fraction boiling at 93 °C collected[140]. The acetyl cyanide obtained (27 g, 0.393 mol) was dissolved in 100 mL of dry benzene, 43 g (0.55 mol) of acetyl chloride were added and the solution cooled in ice. To this ice cold mixture 43.5 g, (0.55 mol) of pyridine dissolved in 100 mL of benzene was added and the mixture was stirred for 24 hours. It was then filtered and the residue washed with benzene. The filtrate was washed with water three times and dried over $MgSO_4$. On rotary vacuum evaporation 43 g of an orange oil[141] was obtained. Distillation of this gave 1-cyanovinyl acetate as a colourless liquid b.p. 72-75 °C, 23 g (52%).

Cyclopentadiene adduct of 1-cyanovinyl acetate



1-Cyanovinyl acetate (11.1 g, 0.1 mol) was refluxed in 60 mL of anhydrous ether with 33 g (0.5 mol) of freshly distilled cyclopentadiene and 22 g of lithium perchlorate for four hours[142]. The yield of adduct obtained was 16.6 g (93%).

2-Norbornenone[143]



(5.2.13)

The cyclopentadiene adduct (1.77 g, 10 mmol) was dissolved in 10 mL of anhydrous methanol under nitrogen. To this was added, with stirring, 20 mL of 2M molar sodium methoxide and stirring was continued for 2.5 hours. After this time 20 mL of 10% NaCl solution was added and the ketone product was extracted 3 times with 20 mL of dichloromethane. The dichloromethane layer was dried over anhydrous magnesium sulfate and evaporation of the solvent under reduced pressure yielded 0.73 g (68%) of 2-norbornenone. The ketone was further purified by silica column chromatography using petroleum ether:ethyl acetate, 75:25 as eluent. The first fraction off the column was the ketone.

^{1}H NMR (500 MHz,$CDCl_3$), δ 3.18 (s,1H, H1), 6.57 (dd, 1H J = 2.9, 5.4 Hz, H2), 6.11 (t, 1H J = 4.4 Hz, H3), 3.01 (d,1H J = 1.5 Hz, H4), 2.19 (dd, 1H J = 4.4, 4.9 Hz, H5x), 1.99 (d,1H J = 9.3 Hz, H5n), 1.93 (d, 1H J = 2.9 Hz, H7a), 1.84 (dd, 1H J = 4.4 Hz,H7s).

^{13}C NMR (75 MHz, $CDCl_3$), δ 39.93 (C1), 142.97 (C2), 130.45 (C3), 55.73 (C5), 215.63 (C5,CO), 50.80 (C6), 37.13 (C7).

Method B

In this method 5-hydroxy-2-norbornene, available as a mixture of *endo* and *exo* isomers, was oxidised to 2-norbornenone. The oxidising agent used was pyridinium chlorochromate. The oxidation was carried out under two sets of conditions.

Preparation of Pyridium chlorochromate[144,145]

To a solution of 12 g (0.12 mol) of chromium trioxide in 22 mL of 6M HCl in a R.B. flask kept in a water bath at 40 °C, 9.5 0 g of pyridine was added slowly over 10 minutes with constant stirring. The mixture was then kept at 10 °C until an orange yellow solid formed. It was then reheated to 40 °C and 10 g of alumina added with stirring. The mixture was dried under high vacuum for 12 hours and stored under argon in the dark.

Oxidation of 5-hydroxy-2-norbornene (Method 1)

1. 0 g of the 5-norbornen-2-ol mixture (Aldrich) was dissolved in 20 mL of anhydrous CH_2Cl_2. This was then added, as single quantity, to a suspension of 25 g (20 mmol) of the pyridinium chlorochromate/alumina mixture in 20 mL of anhydrous CH_2Cl_2. About 5 minutes after the addition of alcohol the colour darkened.The mixture was stirred at room temperature for 6 hours[145]. The solid residue was then filtered using a sintered crucible and the residue washed with ether. Evaporation of the filtrate under reduced pressure gave the ketone as a light yellow oil. This ketone was further purified by silica column chromatography (1:20) using as eluent 75:25 petroleum ether:ethyl acetate. The yield of norbornenone was obtained was 0.69 g (77%).

Oxidation of 5-hydroxy-2-norbornene (Method 2)[28]

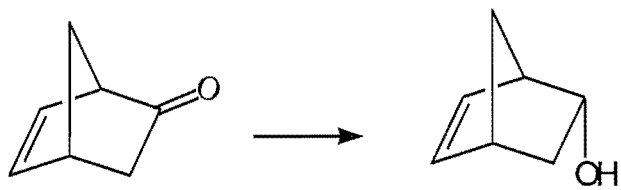
Dry dichloromethane (35 mL) and anhydrous pyridine (4.3 mL) were placed in a two necked 250 mL R.B.flask. CrO_3 (2.7 g) was added to this in small portions with constant stirring[146,147]. When all CrO_3 had dissolved the solution becomes dark brown[148]. To this solution 500 mg (4.5 mmol) of the 5-norbornen-2-ol (Aldrich) sample dissolved in 14 mL of anhydrous dichloromethane was

added all at once, and the solution was further stirred for 20 minutes.[110] The reaction was tested for completeness by TLC. The reaction mixture was then filtered through a short Celite 545 column, and washed with dichloromethane. The combined filtrates were washed with 5% aqueous KOH (20 mL), 5% aqueous HCl (20 mL), saturated $NaHCO_3$ solution (20 mL) and finally with saturated brine solution (20 mL). They were dried by filtration through a sintered funnel containing anhydrous Na_2SO_4 and the solvent removed under reduced pressure. The residue was chromatographed on silica column (1:20) using eluent pentane: ether, 7:3; as eluent. The first fraction was pure 2-norbornenone. The yield was 0.420 mg, (84%). The NMR spectrum was identical to that for the earlier preparation.

Reduction of 2-norbornenone

Two methods were used for the reduction of norbornenone. Both used sodium borohydride as the reducing agent. The second method gave better yields.

Method 1[146]



(5.2.14)

Norbornenone (0.45 g, 4.2 mmol) was dissolved in 10 mL of anhydrous methanol and added to a suspension of 190 mg (4.2 mmol) of sodium borohydride in methanol kept at -15 °C over a period of 45 minutes. The mixture was then allowed to warm to 0 °C over 1 hour, and kept at this temperature for a further hour. Excess borohydride was destroyed by the addition of 15% aqueous hydrochloric acid until a pH of 5 was reached. Then the methanol was then removed on a rotary evaporator and the alcohol was extracted from the residue with ether (20 mL × 3). The ether solution was dried over $MgSO_4$ and the ether evaporated. The yield of *endo* alcohol obtained was 237 mg (53%).

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.82 (s, 1H, H1), 6.45 (dd, 1H J = 2.9, 5.9 Hz, H2), 6.06 (dd, 1H J = 2.9, 5.9 Hz, H3), 2.99 (s,1H, H4), 4.54 (m, 1H J = 3.4, 3.9, 7.3, 11.2 Hz, H5x), 0.76 (tt,1H J = 2.9 ,3.4, 5.9 Hz, H6n), 2.10 (m, 1H J = 3.4, 3.9, 7.8 Hz, H6x), 1.48 (m, 1H J = 1.5, 2.9, 8.8 Hz, H7s), 1.28 (t, 1H J = 8.8 Hz, H7a).

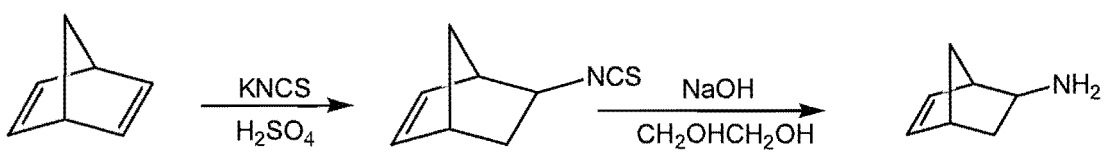
^{13}C NMR (75 MHz, $CDCl_3$), δ 42.86 (C1), 140.41 (C2), 130.79 (C3), 48.07 (C4), 72.46 (C5), 37.76 (C6, CH_2), 48.26 (C7, CH_2).

Method 2[110]

In this method the norbornenone (690 mg, 6.3 mmol) was dissolved in 20 mL of anhydrous methanol and the solution cooled to –15 °C. To this 400 mg of sodium borohydride was added in two equal portions over 30 minutes and the solution was stirred for 1 hour. Sodium bicarbonate solution (20 mL of 5%) was added and the *endo* alcohol product was extracted from this with ethyl acetate (3 x 100 mL). The ethyl acetate extract was dried over $MgSO_4$, and the solvent removed using a rotary evaporator. The residue was columned on silica column using petroleum ether:ethyl acetate, 1:1 as eluent. The yield obtained was 620 mg (84%).

5.2(x) Preparation of 5-*exo*-amino-2-norbornene[149-151]

The above compound was prepared by hydrolysis of the *exo* isothiocyanate, which was obtained by addition of isothiocyanic acid to one of the double bonds of norbornadiene.



(5.2.15)

To a mixture of norbornadiene (20 mL, 0.19 moles) and potassium thiocyanate (19.2 g, 0.20 moles) in 50 mL of benzene, a solution of 7 mL of concentrated sulphuric acid in 4 mL of water was added over a period of two

hours, the temperature being maintained at 38-40 °C. After the addition was complete the mixture was stirred for a further 3 hours. It was then cooled and allowed to stand overnight. Water (200 mL) and ether (200 mL) were then added and the mixture shaken. The mixture was filtered through a sintered glass funnel and the ether layer separated and dried over anhydrous $MgSO_4$. Evaporation of the ether gave a yellow liquid. Distillation of this under reduced pressure gave 18.9 g (66%) of pure isothiocyanate.

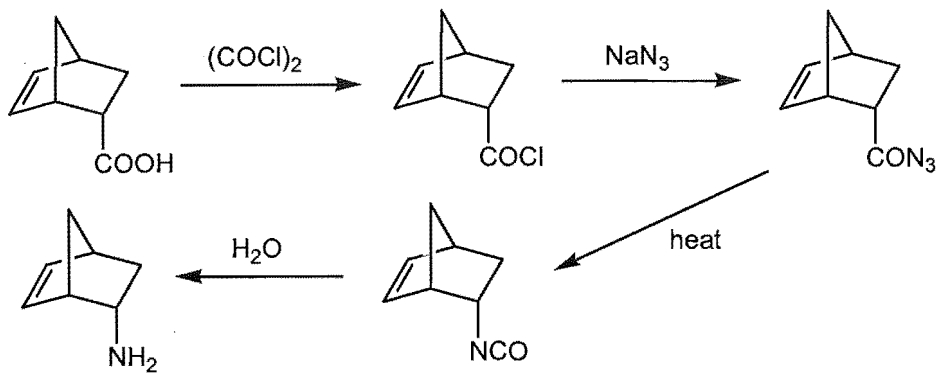
^{1}H (300 MHz, $CDCl_3$),δ 2.96(d, 1H J = 1.0 hz), 6.22(dd, 1H J = 2.9, 5.4 Hz), 5.97(dd, 1H J = 3.4,5.9 Hz), 3.53(t,1H J = 5.9, 11.2 Hz), 3.07(dd, 1H J = 2.4, 3.9 Hz), 2.96(d, 1H J = 1.0 hz), 1.66-1.71(m, 4H).
^{13}C (75 MHz, $CDCl_3$),δ 140.25, 132.75, 55.31, 49.81, 46.17, 41.06, 35.62.

The 5-*exo*-isothiocyanato-2-norbornene (18.92 g, 0.125 mol) was added to 160 mL of ethylene glycol at 100 °C, then solid sodium hydroxide (15 g, 0.375 mol) was added over 5 minutes with constant stirring, the temperature being maintained at 95-100 °C. The temperature was then raised to 160-167 °C and stirring continued for three hours. The mixture was kept overnight and then added to one litre of saturated potassium carbonate solution. The amine was taken up in dichloromethane (4 x 100 mL) and extracted from the dichloromethane with 2M HCl. The aqueous acid layer was separated and the amine precipitated by addition of 2M NaOH solution, followed by saturated potassium carbonate. The liberated amine was extracted from the aqueous layer with ether (100 mL x 5) dried over anhydrous $MgSO_4$. Evaporation of the ether gave 10.27 g of amine. A ^{1}H NMR spectrum showed this amine to be pure 5-*exo*-amino-2-norbornene. The overall yield was 55%.

^{1}H NMR (300 MHz, $CDCl_3$), δ 2.50 (s, 1H, H1) 6.08 (dd, 1H *J* = 2.8, 5.9 Hz, H2), 6.02 (dd, 1H J = 3.2, 5.9 Hz, H3), 2.79 (s, 1H, H4), 2.89 (td, 1H J = 2.8, 3.2, 7.5 Hz, H5), 1.57 (td, 1H J = 3.2, 4.8, 8.7 Hz, H6x), 1.49 (t, 1H J = 4.4 Hz, H6n), 1.60 (d, 1H J = 2.8 Hz, H7s), 1.06 (tt, 1H J = 3.2, 3.6 Hz,H7a).
^{13}C NMR (75 MHz, $CDCl_3$),δ 41.17 (C1), 138.06 (C2), 134.99 (C3), 50.71 (C4), 51.85 (C5), 44.82 (C6), 36.86 (C7).

5.2(xi) Preparation of 5-*endo*-amino-2-norbornene

This compound was prepared by the Curtius rearrangement of 2-norbornene-5-*endo*-carboxylic acid.[152-154]



(5.2.16)

2-Norbornene-5-*endo*-carboxylic acid (1 g, 7.2 mmol) was dissolved in 20 mL of dry dichloromethane. To this solution, oxalyl chloride (4 mL, 0.044 mol) was added and the whole refluxed for 3 hours. The solvent was then removed under reduced pressure. The residual oil was mixed with 40 mL of acetone (previously dried over 4A molecular sieves for 24 hours) and sodium azide (4 g, 0.061 moles) and the mixture refluxed on a water bath at 70 °C for 2 hours. The residue was then removed by filtration through a sintered crucible and the residue washed with acetone. The acetone solvent was removed by vacuum evaporation and the residue was refluxed in 50 mL of dry toluene for six hours. Dilute hydrochloric acid (1:1, 50 mL) was added and the mixture refluxed to extract the amine into the aqueous phase. The aqueous layer was then separated and made alkaline with 20% sodium hydroxide solution. The precipitated amine was extracted with ether (50 mL×3) the solution dried over anhydrous $MgSO_4$ and the ether evaporated. The yield of *endo* amine was 0.41 g (53 %.)

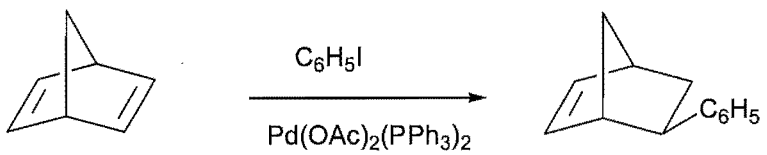
^{1}H NMR (300 MHz, $CDCl_3$), δ 2.60(s, 1H, H1), 6.37 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.99(dd, 1H J = 2.9, 5.9 Hz, H3), 3.06 (s, 1H, H4), 2.86(s, 1H, H5), 2.22(dt, 1H J

= 3.4, 4.9, 8.8, 12.2 Hz, H6x), 1.49(m, 1H J = 3.4, 4.4, 12.2 Hz, H6n), 1.33(t, 1H J = 5.4, 9.3 Hz, H7a), 0.70(tt, 1H J = 2.9, 3.4, 5.9 Hz, H7s).

^{13}C NMR (75 MHz, $CDCl_3$), δ 42.50 (C1), 140.37 (C2), 131.20 (C3), 48.67 (C4), 50.98 (C5), 46.13 (C6), 35.44 (C7).

5.2(xii) Preparation of 5-*exo*-phenyl-2-norbornene.[155-157]

This was prepared in 95% yield by the coupling reaction between norbornadiene and iodobenzene using a palladium acetate-triphenylphosphine complex catalyst. [The catalyst was prepared by stirring palladium acetate (225 mg) and triphenyl phosphine (524 mg) (1:1 molar ratio) in acetonitrile at room temperature for 20 minutes. The yellow precipitate formed was filtered off and dried in a desiccator.]



(5.2.17)

In a small round-bottomed flask containing 5 mL of dry dimethyl sulfoxide under argon, norbornadiene (1.095 g, 11.9 mmol) and iodobenzene (0.816 g, 4 mmol) were added. To this mixture 166 mg (0.22 mmol) of the catalyst was introduced, followed by triethylamine (1.9 mL, 11.6 mmol) and formic acid (0.4 mL, 13.6 mmol). The mixture was heated on water bath at 60 °C for 18 hours. It was then extracted with pentane (3 x 20 mL). The combined pentane fractions were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The 5-*exo*-phenyl-2-norbornene (740 mg, 95%) obtained was further purified by passing through a dry silica column (1:50), using petroleum ether as eluent. The second fraction consisted of pure 5- *exo*- phenyl-2-norbornene (740 mg, 84%).

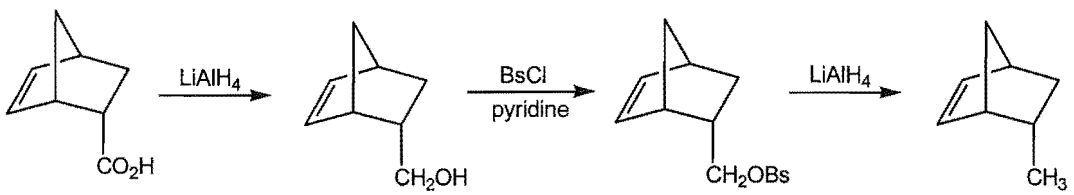
^{1}H NMR (500 MHz, $CDCl_3$), δ 7.31 (d, 1H J = 2.0 Hz), 7.28 (m, 2 H J = 2.0, 2.4, 6.3, 8.3 Hz), 7.17 (m, 2 H J = 2.4, 3.4, 5.4, 8.8 Hz), 2.96 (s, 1H , H1), 6.16 (dd, 1H J = 2.9, 5.9 Hz, H2), 6.25 (dd, 1H J = 2.9, 5.4 Hz, H3), 2.91 (d, 1H J = 1.0 Hz, H4), 2.72 (dd, 1H J = 4.9, 8.3 Hz, H5n), 1.74 (m, 1H J = 3.4, 4.4, 7.8, 11.7 Hz,

H6x), 1.63 (m, 1H J = 2.9, 3.4, 11.7 Hz, H6n), 1.58 (d, 1H J = 8.3 Hz, H7a), 1.43 (m, 1H J = 1.5, 5.9, 8.8 Hz, H7s).

^{13}C NMR (75 MHz, $CDCl_3$), δ 42.27 (C1), 137.33 (C2), 137.27 (C3), 48.17 (C4), 43.68 (C5), 33.65 (C6), 45.73 (C7), Phenyl: 125.49, 127.0, 128.22, 146.14.

5.2(xiii) Preparation of 5-*endo*-methyl-2-norbornene.

5-*Endo*-methyl-2-norbornene was prepared from the *endo* carboxylic acid by the literature procedure below.[125,158,159]



[BsCl = 4-$BrC_6H_4SO_2Cl$]

(5.2.18)

2-Norbornene-5-*endo*-carboxylic acid (1 g, 7.2 mmol) was dissolved in 30 mL of anhydrous ether and added in small portions, with stirring, to a solution of lithium aluminium hydride (0.69 g, 0.024 mol) in 30 mL of ether cooled in ice. After addition was complete, the mixture was refluxed for four hours. The excess hydride was broken down by the cautious addition of 20 mL of saturated NH_4Cl (5 g in 20 mL of water), followed by 20 mL of saturated NaCl solution. The product was then extracted with ether (40 mL x 3). The ether layer was washed once with 10 mL of 10% Na_2CO_3 solution to remove any unreacted acid and then with water. Finally it was dried over anhydrous $MgSO_4$ and the ether evaporated. The yield of alcohol was 0.40 0 g (45%).

^{1}H NMR (300 MHz, $CDCl_3$),δ 2.70(d, 1H J = 1.0 hz), 6.11(dd, 1H J = 2.9, 5.9 Hz), 5.93(dd, 1H J = 2.9, 5.9 Hz), 2.90(s, 1H), 3.36(q,1H J = 6.3, 6.8, 10.2 Hz), 3.21(q, 1H J=8.8, 10.3 Hz), 2.26(m,1H J=1.5, 2.4, 4.4, 9.3 Hz), 2.07 (d, 1H J =1.5 Hz), 1.79(4d, 1H J = 2.4, 3.9, 9.3 Hz), 1.42(m, 1H J = 4.4, 8.3, 12.7 Hz), 1.23(d, 1H J = 8.3 Hz), 0.49(dt, 1H J = 2.4, 4.4, 6.8, 11.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$), δ 41.53(C1), 137.32(C2), 132.08(C3), 42.12(C4), 49.43(C5), 28.70(C6), 43.48(C7), 66.30(C8, CH_2OH).

This product was shaken with a mixture of 1 g (3.9 mmol) of 4-$BrC_6H_4SO_2Cl$ and 5 mL of pyridine and then warmed on a water bath at 70 °C for 1 hour. The excess pyridine was removed under reduced pressure and the residue was dissolved in 30 mL of anhydrous ether. To this 3 mL of a solution of 1M lithium aluminium hydride in tetrahydrofuran was added and the mixture refluxed on a water bath at 80 °C for 1 hour. It was then allowed to stand overnight. The excess lithium aluminium hydride was broken down by the addition of 50 mL 5M cold dilute sulphuric acid. The crude 5-*endo*-methyl-2-norbornene product was then extracted from this using ether (40 mL x 4). The milky coloured ether layer then washed with 10% Na_2CO_3 (20 mL × 2), and then twice with water. The clear ether layer was then dried over $MgSO_4$ and evaporated to give 309 mg of 5-*endo*-2-norbornene (40%).

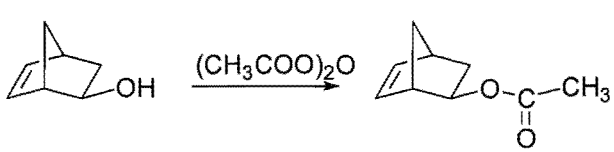
^1H NMR(300 MHz, $CDCl_3$),δ 2.80(s,1H), 6.14(dd, 1H J= 2.9, 5.9 Hz), 5.96(dd, 1H J = 2.9, 5.4 Hz), 2.93(s,1H), 3.75(m, 1`H J = 2.4, 3.9, 6.3, 8.7 Hz), 2.29(m, 1H J = 3.9, 6.3, 7.8, 9.8 Hz), 1.45 (td, 1H J = 3.9, 5.9, 9.8 Hz), 2.04(d, 1H J = 5.4 Hz), 0.52(4d, 1H J = 2.4, 2.9, 4.9, 7 3 Hz), 1.86 (4d, 1H J = 2.9, 3.9, 6.8, 9.8 Hz).

^{13}C NMR (75 MHz, $CDCl_3$), δ 41.56(C1), 137.29(C2), 132.09(C3), 49.41(C4), 28.70(C5), 42.10(C6), 43.48(C7), 25.52(CH_3).

5.2(xiv) Preparation of the 5-acetoxy-2-norbornenes

These esters were obtained is ca. 70% yield by acetylation of the corresponding 5-norbornenol using acetic anhydride in pyridine containing a small amount of DMAP as a catalyst.

(a) 5-*exo*-acetoxy-2-norbornene[81,160]

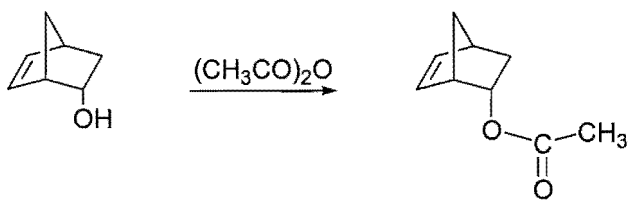


(5.2.19)

5-*exo* hydroxy-2-norbornene (380 mg, 3.5 mmol) was dissolved in 8 mL of anhydrous dichloromethane in a 100 mL R.B.flask under nitrogen. To this solution 0.9 mL (11.2 mmol) of anhydrous pyridine and two small crystals (a catalytic amount) of DMAP (4-dimethylaminopyridine) were added. The solution was then shaken well, 0.6 mL (6.36 mmol) of acetic anhydride was added and the whole was stirred at room temperature under nitrogen for 24 hours. The mixture was then quenched by adding 10 mL of water. The ester product was extracted into CH_2Cl_2 (40 mL × 4) and the combined extracts were then washed successively with 10 mL each of saturated copper sulphate solution, water and brine. The organic layer was then dried over anhydrous $MgSO_4$ and the solvent evaporated. The crude product was further purified by passing through a dry silica column (1:30) using petroleum ether: ethyl acetate (95:5) as eluent. The first fraction obtained was pure 5-*exo*-acetyl-2-norbornene. The yield was 0.366 g (70%).

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.82 (s, 1H, H1), 6.23 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.95 (dd, 1H J = 2.9, 5.4 Hz, H3), 2.88 (s, 1H, H4), 4.65 (d, 1H, J = 7.0 hz, H5n), 1.69 (m, 1H J = 2.9, 3.9, 6.8 Hz, H6x), 1.57 (dd, 1H J = 1.5, 8.3, 9.8 Hz, H6n), 1.65 (d, 1H J = 7.8 Hz, H7s), 1.36 (dd,1H J = 2.0, 8.8 Hz, H7a).
^{13}C NMR (75 MHz, $CDCl_3$), δ 46.06 (C1), 141.06 (C2), 132.61 (C3), 47.48 (C4), 75.06 (C5), 40.45 (C6), 47.10 (C7), 21.25 (CH_3), 170.97 (CO).

(b) 5-*endo*-acetoxy-2-norbornene



(5.2.20)

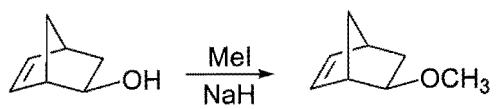
5-*endo*-Acetoxy-2-norbornene was prepared from 5-*endo*-hydroxy-2-norbornene using the same method as that used for the *exo* isomer. The crude product was purified by silica column (1:30) using as eluent petroleum ether:ethyl acetate (95:5). The first fraction obtained was pure 5-*endo*-acetoxy-2-norbornene. The yield was 0.375 g (72%).

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.82 (s, 1H, H1), 6.31 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.96 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.11 (s, 1H, H4), 5.25 (dt, 1H J = 2.9, 3.4, 7.8 Hz, H5x), 2.12 (m, 1H J = 3.4, 3.9, 4.4, 7.8 Hz, H6x), 1.45 (tt, 1H J = 1.5, 2.0, 3.4, 5.4 Hz, H6n), 1.30 (d, 1H J = 8.8 Hz, H7s), 0.90 (dt, 1H J = 3.4, 6.3 Hz, H7a). ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.04 (C1), 138.34 (C2), 131.39 (C3), 47.49 (C4), 74.94 (C5), 45.58 (C6), 34.40 (C7), 20.99 (CH3), 171.13 (CO).

5.2(xv) Preparation of the *exo*- and *endo*-5-methoxy-2-norbornenes.

Initially an attempt was made to prepare 5-*exo*-methoxy-2-norbornene by the oxymercuration-demercuration of one of the double bonds in norbornadiene in methanol solution[158]. A product was obtained in 46% yield, but this proved to be a mixture of the *endo* and *exo* isomers present in a ratio of 68:32. Rather than attempt to separate these, both isomers were instead prepared from the corresponding 5-*exo* or 5-*endo*-hydroxy-2-norbornene by converting them to their sodium salts and methylating these with methyl iodide.

(a) 5-*exo*-methoxy-2-norbornene[81]



(5.2.21)

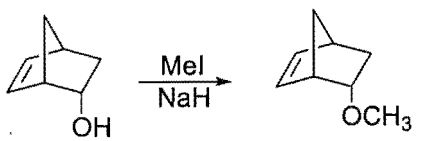
Sodium hydride 0.135 g (5.58 mmol) was washed with pentane, dried under nitrogen and suspended in 5 mL of anhydrous THF cooled in ice. To this suspension 410 mg (3.72 mmol) of 5-*exo*-hydroxy-2-norbornene. The stirred mixture was then refluxed on a water bath at 50-55°C for three hours. It was then cooled to room temperature; 1.58 g (11.1 mmol) of iodomethane added, and the contents of the flask stirred for twelve hours at room temperature. At this point it was quenched with aqueous NH_4Cl (1 g in 5 mL water) and the product extracted with diethyl ether (10 mL × 3). The ether extract was washed with brine (10 ml), dried over anhydrous $MgSO_4$, and the ether evaporated. The crude product was

obtained as a colourless liquid (0.315 g, 68%). It was purified by passing through a silica column (1:30) using petroleum ether:ether, 90:10 as eluent.

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.77 (s, 1H, H1), 6.16 (dd, 1H, J = 2.9, 5.9 Hz, H2), 5.90 (dd, 1H J = 3.4, 5.4 Hz, H3), 2.88 (s,1H, H4), 3.36 (m, 1H J = .1.5, 2.9, 4.9, 9.3 Hz H5n), 1.54 (t, 1H J = 2.4, 6.3, 9.3 Hz, H6n), 1.62(d, 1H J = 7.8 Hz, H6x), 1.52(dd, 1H J = 2.4,3.9 Hz, H7s), 1.30(dt, 1H J = 2.4, 2.9, 5.9 Hz H7a), 3.31 (m, 3H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$), δ 40.30 (C1), 140.59 (C2), 133.10 (C3), 45.82 (C4), 82.00 (C5), 45.82 (C6), 34.16 (C7), 56.72 (OCH_3).

(b) 5-*endo*-methoxy-2-norbornene



(5.2.22)

This was prepared by essentially the same method starting from *endo*-5-hydroxy-2-norbornene. The norbornenol (0.300 g, 2.73 mmol) was added to an ice cold suspension of sodium hydride (0.135 g (5.58 mmol) in 4 mL of anhydrous THF. The mixture was then stirred for 30 minutes and then refluxed on a water bath at 50° for three hours. It was then cooled and 2.5 g (17 mmol) of iodomethane was added. The mixture was then stirred for 48 hours, before quenching with 10 mL (1 g) ammonium chloride solution. The *endo* methoxynorbornene was then extracted with diethyl ether (40 ml × 4), the ether extract washed with 10 ml of brine solution, dried over anhydrous $MgSO_4$, filtered and the ether evaporated. This crude product (0.319 g) was further purified by silica column using eluent petroleum ether:ether, 1:1. Pure 5-*endo*-methoxy-2-norbornene (0.215 g, 64% yield) was obtained as the first fraction to come off the column.

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.79(s, 1H, H1), 6.30 (dd, 1H J = 2.9, 5.3 Hz, H2), 5.98 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.10 (s, 1H, H4), 4.06 (dt, 1H J = 2.9, 3.4, 7.8 Hz, H5x), 1.96 (m, 1H J = 3.9, 4.4, 7.8, 12.2 Hz, H6x), 0.88 (td, 1H J = 3.4, 5.9,

12.2 Hz, H6n), 1.44 (m, 1H J = 1.5, 2.9, 8.3 Hz, H7s),1.23 (d, 1H J = 8.3 Hz, H7a), 3.27 (s,3 H, OCH_3).

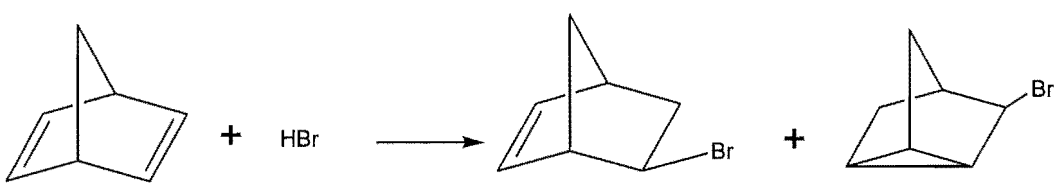
^{13}C NMR (75 MHz, $CDCl_3$), δ 42.16 (C1), 138.06 (C2), 131.20 (C3), 47.28 (C4), 81.67 (C5), 44.99 (C6), 34.03 (C7), 56.70 (OCH_3).

5.2(xvi) Preparation of the 5-*exo*-halogeno- 2-norbornenes

No attempt was made to prepare 5-fluoro-2-norbornene, and it only proved possible to obtain the *exo*-forms of the 5-chloro-, 5-bromo- and 5-iodo derivatives. Preparations of all of these contained about 23-27% of the isomeric 3-X-nortricyclene. Attempts were made to rid the sample from this by HPLC. They were successful for the *exo*-5-iodo and *exo*-5-bromo compounds, but not for the *exo*-5-chloro. *exo*-5-Chloro and *exo*-5-bromo-2-norbornene were prepared by passing dry gaseous HCl and HBr respectively through a solution of norbornadiene in methylene chloride at –78°C.

(a) 5-*exo*-bromo-2-norbornene

Method A[161,162].



(5.2.23)

Norbornadiene (10.8 mL, 0.100 mol) was dissolved in 50 mL of anhydrous dichloromethane and to this 2.5 g of silica gel was added. The mixture was then cooled to -78°C. Through this mixture dry hydrogen bromide (generated by the addition of 63% hydrobromic acid to concentrated sulphuric acid) was passed for two hours. The solution was then stirred for 10 minutes. Excess HBr

was removed by passing nitrogen through the solution and this was then stored overnight at room temperature. The silica gel was filtered off and the organic layer washed with water (50 ml), saturated sodium bicarbonate solution (50 ml), and again with water. It was then dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. Approximately 9.3 g of material was obtained. N.M.R. analysis showed that this consisted of a mixture of 77% 5-*exo* bromo-2-norbornene and 23% 3-*exo*-bromonortricyclene.

5-*exo*-bromo-2-norbornene

^1H NMR (500 MHz, $CDCl_3$),δ 2.90 (s,1H ,H1), 6.19 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.98 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.10 (d, 1H J = 1.5 Hz, H4), 3.77 (dt, 1H J = 2.4, 4.9, 7.3 Hz,H5n), 2.01 (m, 1H J = 3.4, 4.4, 7.8 Hz, H6x), 1.64 (m, 1H J = 2.4, 3.4, 7.8 Hz, H6n), 1.88 (dt, IH J = 2.4, 3.9, 5.9, 8.8 Hz, H7a), 1.36 (m, 1H J = 1.5, 5.9, 7.8 Hz, H7s).

^{13}C NMR (75 MHz, $CDCl_3$), δ 42.14 (C1), 139.80 (C2), 133.27 (C3), 49.18 (C4), 51.68 (C5), 46.18 (C6), 38.25 (C7).

3-*exo*-bromonortricyclene

^1H NMR (500 MHz, $CDCl_3$), δ 3.94, 2.11, 1.85, 1.55, 1.45, 1.42, 1.25, 1.22, 0.87

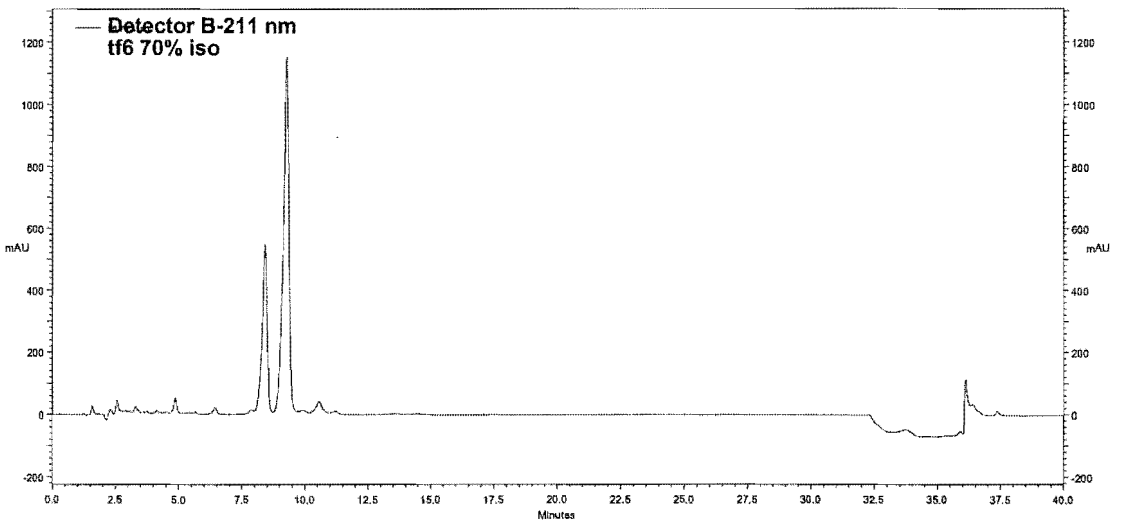
^{13}C NMR (75 MHz, $CDCl_3$), δ 11.56 (C1), 13.90 (C2), 57.36 (C3), 37.16 (C4), 31.44 (C5), 18.15 (C6), 30.96 (C7).

Method B[163,164]

This method was also used and it proved much more convenient than the previous one. It is a modified addition of hydrogen halide to double bonds. Norbornadiene 2.0 g (0.021 mol) was dissolved in 25 mL of dichloromethane. To this solution was added 5.0 g (0.042 mol) of potassium bromide, followed by 15.0 g of orthophosphoric acid. The mixture was then stirred at room temperature for 18 hours. It was then diluted with 100 mL of water and the dichloromethane layer separated. This was washed with 20 mL of sodium carbonate solution three times, separated, dried over anhydrous $MgSO_4$ and the solvent evaporated to give 2.28 g of product that proved to be a mixture of 5-*exo*-bromo-2-norbornene and 3-

exo-bromo nortricyclene in the ratio 35:65. This was purified by passing through a silica column using petroleum ether as eluent. The first fraction off the column was unreacted norbornadiene. This was followed by a pure mixture of 5-*exo*-bromo-2-norbornene and 3-*exo*-bromonortricyclene of the same (77:23) composition as before. The proton and carbon NMR were identical to those obtained earlier using method A.

HPLC separation of 5-*exo*-bromo-2-norbornene and 3-*exo*-bromo nortricyclene.



Mixture of 5-*exo*-bromo-2-norbornene and 3-*exo*-bromonortricyclene

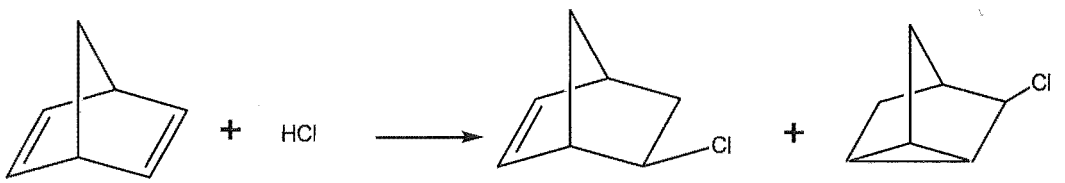
(5.2.24)

From the analytical HPLC it was determined that most suitable solvent for the separation of 5-exo bromo-2-norbornene and 3-exo bromonortricyclene was 80% acetonitrile-20% water. The mixture was then separated on a preparative HPLC column. A sample of the mixture (50 mg) was dissolved in 1 mL of acetonitrile, injected on to the preparative column 450μL at a time and eluted with 80:20 acetonitrile :water using a flow rate of 10 mL per minute.. The fractions were detected by UV at a wavelength 211nm. The purity of components was determined by NMR.

(b) 5-*exo*-chloro-2-norbornene

The same two methods were used for this as for the *exo*-bromo-2-norbornene.

Method A[161,162]



(5.2.25)

Silica gel (2.5 g) was suspended in 50 mL of dry dichloromethane in a two necked R.B.flask. To this 10.8 mL (0.100 mol) of norbornadiene was added and the mixture cooled to -78 °C. Through this solution hydrogen chloride (liberated by the addition of concentrated sulphuric acid to sodium chloride) was passed for one hour with constant stirring and the solution was then kept at room temperature overnight. The silica was filtered off and the filtrate was then washed with water (30 mL), saturated sodium bicarbonate (20 mL) solution, and finally with water (30 mL) once more. It was then separated, dried over anhydrous $MgSO_4$ and the solvent removed under reduced pressure. The product was obtained as 9.42 g of a colourless liquid. This was distilled under reduced pressure (10 mm) and the fraction that came over at 40-42 °C was collected. The weight of product was 5.98 g and NMR analysis showed that it consisted of a mixture of 5-*exo*-chloro-2-norbornene and 3-*exo*-chloronortricyclene in the ratio 75:25.

5-*exo*-chloro-2-norbornene

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.90(s,1H, H1), 6,20(dd, 1H J = 2.9, 5.9 Hz, H2), 5.98(dd, 1H J = 2.9, 5.9 Hz, H3), 2.99(dd, 1H J = 1.6 Hz, H4), 3.78(m,1H J = 3.9, 4.8, 6.7 Hz, H5n), 1.85(dt, 1H J = 3.6, 5.2, 6.7 Hz, H6x), 1.61(m, 1H J =1.5, 3.9, 8.7 Hz, H6n), 1.82(m, 1H J = 1.5, 6.7, 8.7 Hz, H7a), 1.79(t, 1H J = 3.2, 6.3 Hz, H7s).

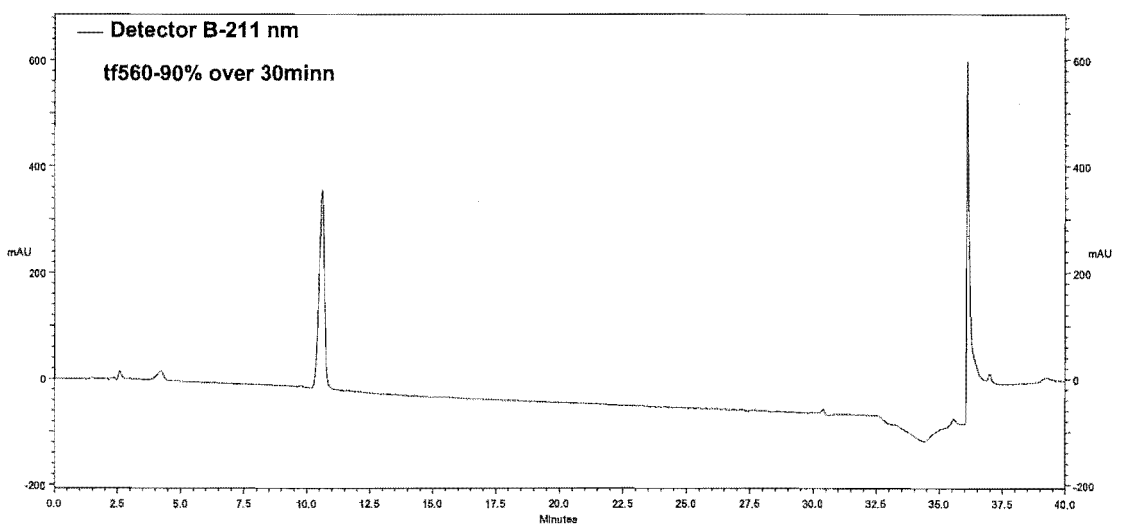
^{13}C NMR (75 MHz, $CDCl_3$), δ 41.62(C1), 140.31(C2), 133.25(C3), 51.36(C4), 58.36(C5), 45.93(C6), 38.14(C7).

Method B[164]

In a R.B.flask 6.0 g (0.08 mol) of potassium chloride, 20.0 g of 85% orthophosphoric acid and 25 mL of dichloromethane were combined. This mixture was stirred and to it was added 2.0 g (0.021 mol) of norbornadiene. Stirring at room temperature was continued for 72 hours. An additional 30 mL of dichloromethane was added and the organic layer separated, washed with saturated sodium carbonate solution (30 mL) and then with 30 mL water. The organic layer was dried over anhydrous $MgSO_4$, filtered and the dichloromethane evaporated. A colourless liquid (2.1 0 gms, 75%) was obtained. This was further purified by silica column chromatography (1:30) using petroleum ether as eluent. The only fraction obtained consisted of a mixture of 5-*exo*-chloro-2-norbornene and 3-*exo*-chloronortricyclene, 73:27.

HPLC separation of 5-*exo*-chloro-2-norbornene and 3-*exo*-chloro nortricyclene.

Attempts to separate the above mixture of 5-*exo*-chloro-2-norbornene and 3-*exo*-chloronortricyclene all failed.

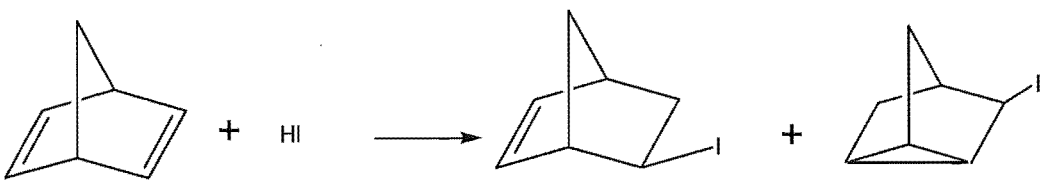


Mixture of 5-*exo*-chloro-2-norbornene and 3-*exo*-chloronortricyclene

(5.2.26)

(c) 5-*exo*-iodo-2-norbornene[163,164]

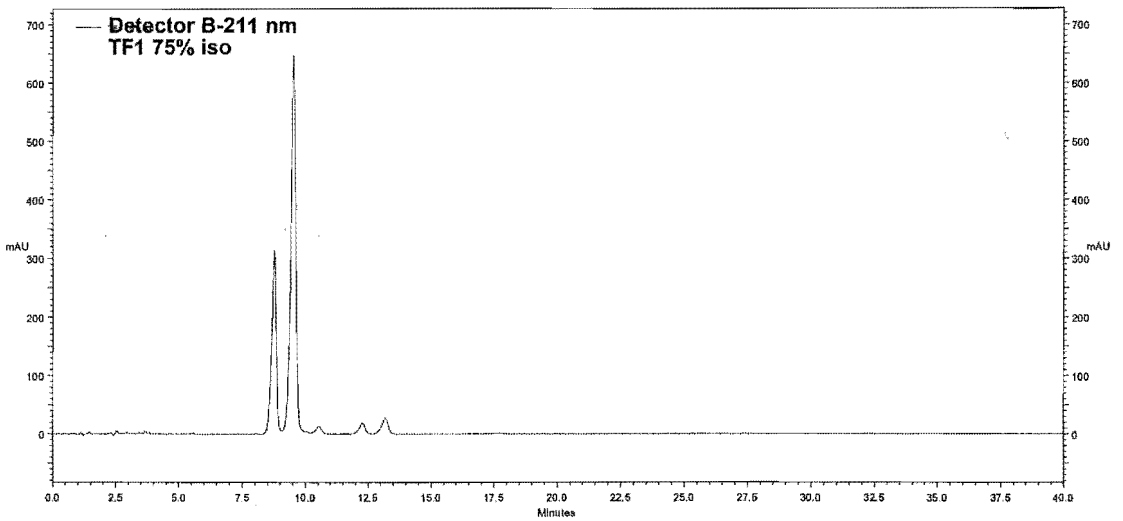
5-*exo*-Iodo-2-norbornene was prepared by reacting norbornadiene with potassium iodide in a mixture of dichloromethane and orthophosphoric acid, a method that had been used previously for the preparation of alkyl iodides from alkenes, and successfully adapted in our case for the corresponding chloro and bromo compounds. As with the latter, the product was accompanied by the nortricylcic isomer.



(5.2.27)

Norbornadiene 2.0 g (0.02 mol) was dissolved in 20 mL of dichloromethane and to this solution 10.0 g (0.06 mol) of potassium iodide and 15.0 g (0.15 mol) of orthophosphoric acid were added. The mixture was vigorously stirred for 4 hours at room temperature. Excess dichloromethane was then added and the organic layer separated. This was then washed with water (30 mL), then with sodium bicarbonate solution until the water was no longer acidic. Finally it was washed with 10% sodium thiosulphate solution to remove iodine, dried over MgSO4 and the solvent evaporated. A colourless liquid (3.55 g) was obtained. The yield varied from 75% to 85%.

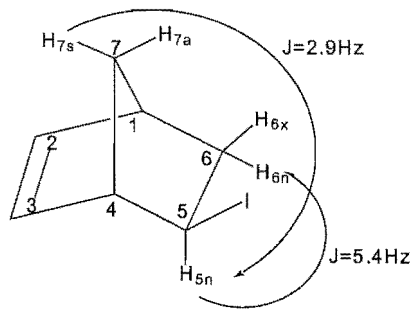
HPLC separation of 5-*exo*-iodo-2-norbornene and 3-*exo*-iodo nortricyclene



Mixture of 5-*exo*-iodo-2-norbornene and 3-*exo*-iodonortricyclene

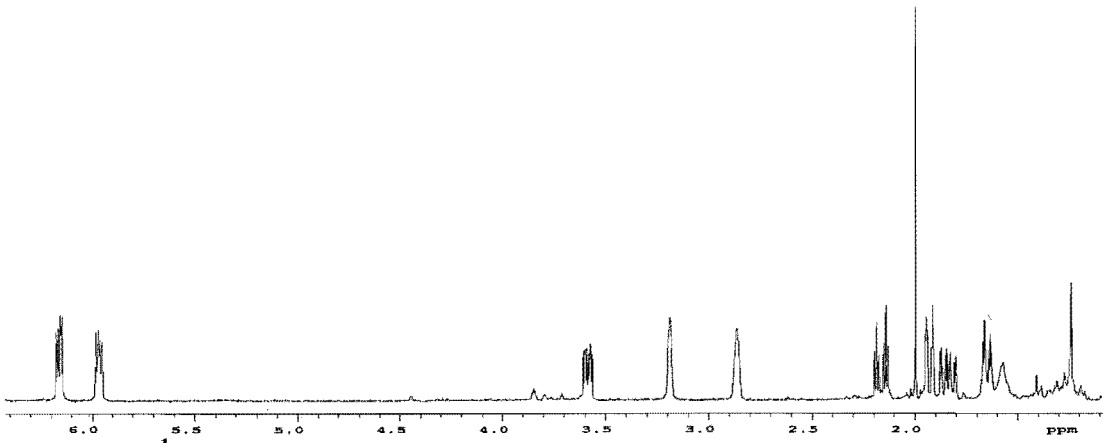
(5.2.28)

From the analytical HPLC a suitable solvent mixture for the separation of 5-*exo*-iodo-2-norbornene and 3-*exo*-iodonortricyclene was found to be 85% acetonitrile/15% water. The mixture was then separated on a preparative HPLC column. A 100 mg sample of the product mixture was dissolved in 2 mL of acetonitrile and injected into the preparative column 250μL at a time. This was then eluted with 85:15, acetonitrile:water mixture. The fractions were detected by UV at a wavelength 210nm. The rate of elution was 12 mL per minute. The separation was successful. The NMR spectra were found to correspond to the two components of the mixture.



5-*exo*-iodo-2-norbornene

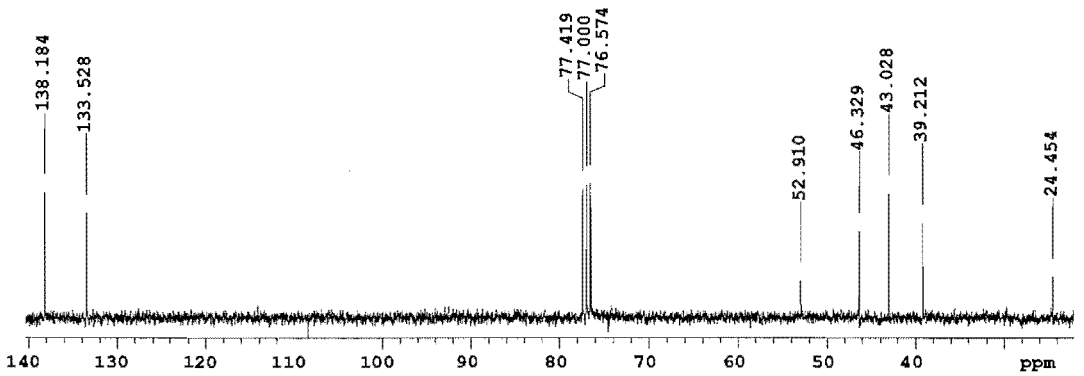
The diagram shows the coupling used for confirming the *exo* nature of iodine addition.



^{1}H NMR of pure 5-*exo*-iodo-2-norbornene after HPLC

5-*exo*-iodo-2-norbornene

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.87 (s, 1H, H1), 6.17 (dd, 1H J = 2.9, 5.4 Hz, H2), 5.98 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.20 (d, 1H J = 1.5 Hz, H4, 3.59 (m,1H J = 2.0, 2.9, 5.4, 9.8 Hz, H5n), 2.17 (dt, 1H J = 3.4, 3.9, 6.3, 13.2 Hz, H6x), 1.85(m, 1H J= 2.4, 5.4, 7.8, 9.8, 13.2 Hz, H6n), 1.97 (dt, 1H J = 1.5, 8.8 Hz, H7a), 1.66 (m, 1H J = 2.4, 3.9, 8.8 Hz, H7s).



^{13}C NMR of pure 5-exo-iodo-2-norbornene after HPLC

^{13}C NMR(75 MHz, $CDCl_3$), δ 43.03(C1), 138.18 (C2), 133.53 (C3), 52.91 (C4), 24.45 (C45), 46.33 (C6), 39.21 (C7).

3-*exo*-iodonortricyclene.

^{1}H NMR (500 MHz, $CDCl_3$), δ 3.80, 2.14, 1.97, 1.54, 1.40, 1.33, 1.33, 1.27, 1.07

^{13}C NMR (75 MHz, $CDCl_3$), δ 37.72, 34.33, 32.24, 30.70, 19.32, 12.95, 11.57.

5.2(xvii) Attempted preparation of 5-*exo*-nitro-2-norbornene.

An attempt was made to prepare 5-exo-nitro-2-norbornene by the oxidation of 5-*exo*-amino-2-norbornene using dioxirane[165,166]. A mixture of unidentified products was obtained.

Chapter 6.

EXPERIMENTAL PART 2: Reactions of 2-norbornenes with phenylselenyl chloride

GENERAL EXPERIMENTAL CONDITIONS

The experimental conditions under which the reaction of phenylselenyl chloride with 2-norbornene and to 5-substituted-2-norbornenes were studied are reported in this section. The solvent used was dichloromethane that had been distilled from calcium hydride and stored over 4A molecular sieves. The products were identified and their relative yields determined by standard NMR techniques (Details on the method used are given in Section 6.5 at the end of this chapter.) An exception was the *endo*- carboxy adduct, the structure of which was confirmed by X-ray crystallography.[102]

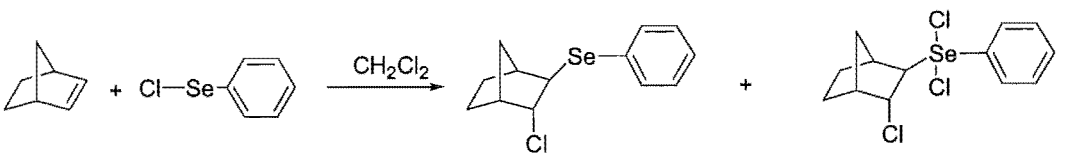
The relative yields of the adducts formed were determined by analysis of ^{1}H NMR spectra of the crude product mixtures formed. These mixtures were subsequently cleaned up by column chromatography. The product obtained off the column was normally a mixture of the two expected isomeric adducts, free of other impurities. However it did not prove possible to separate these two. It was by NMR analysis of these purified mixtures that the individual NMR spectra of the two components were obtained. Any phenyldichloroselanyl derivatives present in the original product mixture did not come off the column.

Initially the reactions of norbornene and norborn-5-ene-2-one with phenylselenyl chloride were studied as models to establish the optimum conditions for the reaction and the analysis of the products. Reaction times were largely based on the time required for the colour of phenylselenyl chloride to disappear from the reaction mixture.

Note:

To make comparison of the results easier, the numbering system used for naming the adducts is based on that for [2.2.1]bicycloheptane, with all substituents present being specified as prefixes. It will frequently differ from that used for the 2-norbornene from which they are derived.

6.1 Reaction of 2-Norbornene with Phenylselenyl Chloride



(40) (54)

Norbornene (40 mg, 0.425 mmol) was dissolved in 2 mL of anhydrous dichloromethane and to this phenylselenyl chloride (104.5 mg, 0.5 mmol) dissolved in 2 ml of anhydrous dichloromethane was added. The solution was stirred for 10 minutes at room temperature. The solution had a pinkish colour at the end due to the slight excess of phenylselenyl chloride present. The solvent was removed under reduced pressure to give 145 mg of yellow oil. ^{1}H NMR of this oil showed it to be a mixture of two products, 2-*endo*-chloro-3-*exo* phenyselanyl[2.2.1]bicycloheptane (**40**) and 2-*endo*-chloro-3-*exo*-phenyldichloroselanyl[2.2.1]bicycloheptane (**54**), present in the ratio of 4:1. Chromatography using a silica column and pure dichloromethane as eluent, gave only (**40**). The other product ((**54**))was retained by the column.

Effect of using excess norbornene

When the above experiment was repeated using 0.130 mmol of norbornene dissolved in 0.5 ml of anhydrous dichloromethane and 0.070 mmol of phenylselenyl chloride, only (**40**) was formed. No (**54**) could be detected.

Effect of temperature

The first reaction was repeated, this time at low temperatures (-120 °C and -78 °C). Under these conditions the same two products were formed, but this time the product ratio was 9:1. On warming this material to 60 °C only the phenylselanyl derivative could be detected.

2-*endo*-chloro-3-*exo*-phenyselanyl[2.2.1]bicycloheptane (40)

^{1}H NMR (500 MHz, $CDCl_3$,),δ 2.45(t, 1H J = 4.0, 8.9 Hz, H1), 4.17 (dt, 1H J = 2.0, 4.4 Hz, H2), 3.12 (t, 1H J = 3.4 Hz, H3n), 2.35 (bd, 1H J = 4.4 Hz,H4), 1.68 (tt, 1H J = 4.9, 9.3 Hz, H5x), 1.36 (m, 1H J = 2.4, 4.4, 4.9, 6.9, 9.3 Hz, H5n) 1.99

(m, 1H J = 2.0, 2.4, 3.9, 4.9, 9.3 Hz, H6n), 1.45 (m, 1H J = 2.0, 2.4, 4.4, 6.3, 9.3 Hz, H6x), 1.79 (d, 1H J = 10.7 Hz, H7s),1.43 (td, 1H J = 1.5, 2.0, 3.4 Hz, H7a), 7.60 (1H), 7.55 (2H), 7.27 (1H).

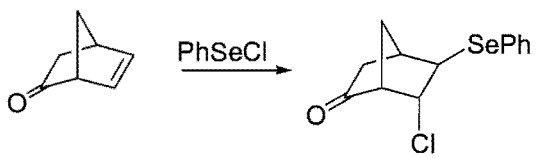
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.56(C1), 67.96(C2), 54.14(C3), 44.41(C4), 29.62(C5), 21.60(C6), 36.26(C7), 129.66(C8), 133.83(C9, C13), 129.04(C10, C12), 127.41(C11).

2-*endo*-chloro-3-*exo*-phenyldichloroselanyl[2.2.1]bicycloheptane (54)

^{1}H NMR (500 Hz, $CDCl_3$),δ 3.21 (d, 1H J = 4.9 Hz, H1), 4.55 (t, 1H J = 2.9, 3.4 Hz, H2x), 5.64 (t, 1H, J = 3.9, 4.4 Hz, H3n), 2.76 (d, 1H J = 3.4 Hz, H4), 1.97 (td, 1H J = 2.0, 2.4, 4.9, 9.3 Hz, H5x), 1.65 (dd, 1H J = 2.9, 4.9, 9.3 Hz, H5n), 2.14 (m, 1H J = 2.0, 2.4, 4.4, 6.8 Hz, H6x), 1.58 (t, 1H J = 4.4, 7.3 Hz, H6n), 2.15 (d, 1H J = 11.2 Hz),H7s), 1.53 (d, 1H J = 9.3 Hz, H7a), 8.22 (1H), 7.54 (2H), 7.24(2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 46.09(C1), 61.60(C2), 83.46(C3), 43.88(C4), 30.99(C5), 21.89(C6), 35.87(C7), 131.60(C8), 131.42(C9, C13), 129.91(C10, C12), 127.65(C11).

6.2 Reaction of Norborn-5-en-2-one with Phenylselenyl Chloride



(56)

Norborn-5-ene-2-one (15 mg, 0.14 mmol) was dissolved in 1 mL of dichloromethane and to this a less than equimolar amount (20 mg, 0.10 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added dropwise. The mixture was then stirred at room temperature for 10 minutes. A portion of the mixture was withdrawn, evaporated under reduced pressure and analysed by NMR. This showed the presence of a single addition product, (**56**). To the remainder of the above mixture a further 15 mg (0.08 mmol) of phenylselenyl chloride dissolved in 0.5 mL dichloromethane was added and the mixture stirred for an additional 10 minutes. The solvent was evaporated under

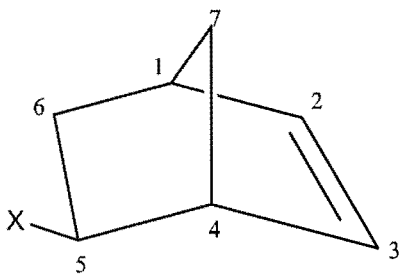
reduced pressure. NMR analysis showed this to be a mixture of (**56**) and its phenyldichloroselanyl analogue in a ratio of 78:22. Chromatography on silica using as eluent petroleum ether:ethyl acetate (90:10)gave some phenylselenyl chloride as a first fraction, followed by pure (**56**) as a single product.

2-*endo* chloro-3-*exo*-phenylselanyl[2.2.1]bicycloheptan-6-one (56)

^{1}H NMR(500 MHz, $CDCl_3$), δ 2.87 (d, 1H J = 3.4 Hz, H1), 4.30 (t, 1H J = 3.4, 7.3 Hz, H2x), 3.44 (t, 1H J = 2.9, 5.9 Hz, H3n), 2.74 (t, 1H J = 1.5, 3.4 Hz, H4), 2.31 (dd, 1H J = 4.9, 5.4 Hz, H5x), 2.06 (dd, 1H J = 4.4 Hz, H5n), 2.21 (dt, 1H J = 1.5, 2.9, 8.3 Hz, H7a), 1.88 (t, 1H J = 1.5, 11.7 Hz, H7s), 7.30-7.34(3H), 7.60-7.62(2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 57.93(C1), 60.49(C2), 52.19(C3), 42.28(C4), 44.71(C5), 208.89(C6), 35.64(C7), 128.52(C8), 134.36(C9, C13), 129.36(C10, C12), 128.16(C11).

6.3 Reactions of 5-*exo*-X-substituted 2-Norbornenes with Phenylselenyl Chloride



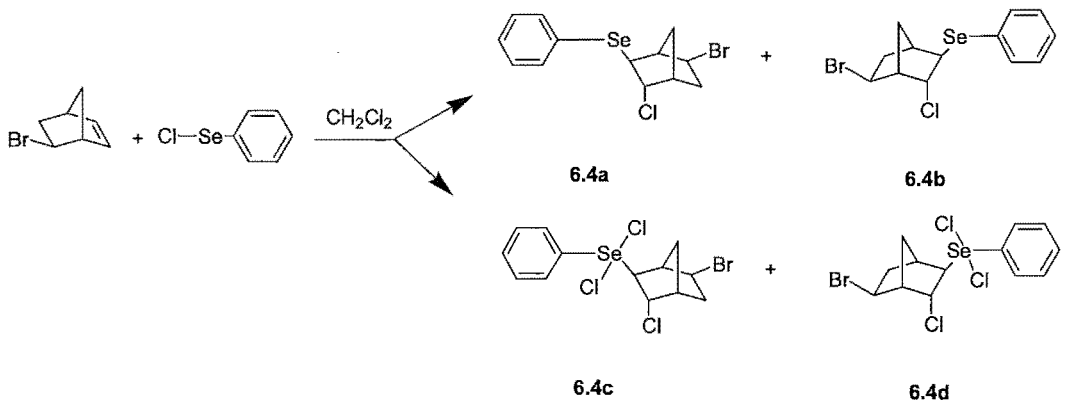
The general method used for norbornene and norborn-5-en-2-one was also adopted for the range of 5-X-norbornenes prepared in Part 1. Because the rates of the addition varied considerably with X, reaction conditions (mostly times) and workup procedures (water bath temperature for the solvent evaporation step) differed slightly. ^{1}H NMR spectra of the crude products and weights of isolated products showed that in most cases the reactions took place in close to quantitative yield. Details of the individual reactions follow.

Note:The chloro and bromo alkenes used, unlike the others, were contaminated with about 25% of the corresponding 3-*exo*-halogenonortricyclene. However

these latter compounds do not react with phenylselenyl chloride. Since both the alkene and the halogenonortricyclenes are considerably more volatile than the adducts, these were lost to the system during the solvent evaporation stage. (The conditions (temperature, pressure) used were aimed at ensuring that this occurred.)

6.3(i) Reactions of 5-e*xo*-bromo-2-norbornene

5-e*xo*-Bromo-2-norbornene (90 mg, 0.466 mmol) was dissolved in 1 mL of dichloromethane and to this 90 mg (0.48 mmol) of phenylselenyl chloride dissolved in 1 ml of anhydrous dichloromethane was added. The mixture was stirred at room temperature for 20 minutes and the solvent removed under reduced pressure. The ^{1}H NMR of the product showed the presence of four products:



The main ones were the two expected, (**6.4a**) and (**6.4b**), formed in 38.5% and 35% yields, respectively. The two minor ones, (**6.4c**) and (**6.4d**) were formed in 17.5% and 9% yields. Chromatography of the crude product on silica, and eluting with petroleum ether gave the unreacted PhSeCl as the first fraction. Subsequent elution with dichloromethane gave an unresolvable mixture of (**6.4a**) and (**6.4b**). As in the norbornene reaction, the phenyldichloroselanyl compounds remained on the column.

The experiment was repeated at -78 °C using excess 5-*exo*-bromo-2-norbornene. Any excess 5-*exo*-bromo-2-norbornene or 3-bromonortricyclene was removed by rotary vacuum evaporation on a hot water bath at 90 °C. This time no

(**6.4c**) and (**6.4d**) could be detected. The (**6.4a**) and (**6.4b**) were present in the same proportions as in the room temperature reaction.

5-*exo*-bromo-2-*endo*-chloro-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.4a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.52 (m, 1H J = 1.5, 4.4, 5.9 Hz, H1), 4.13 (dt, 1H J = 2.0, 4.4 Hz, H2x), 2.97 (t, 1H J = 3.4, 7.3 Hz, H3n), 2.61 (s, 1H H4), 4.00 (dt, 1H J = 2.0, 4.4, 4.9, 7.8 Hz, H5n), 2.84 (td, 1H J = 2.4, 2.9, 11.2 Hz, H6n), 2.04 (m,1H J = 2.4, 4.4, 10.7 Hz, H6x), 2.08 (m, 1H J = 1.5, 3.4, 8.3 Hz, H7s), 1.84 (td, 1H J =1.5, 2.0, 3.4 Hz, H7a), 7.29-7.32 (3H), 7.55-7.60(2H).

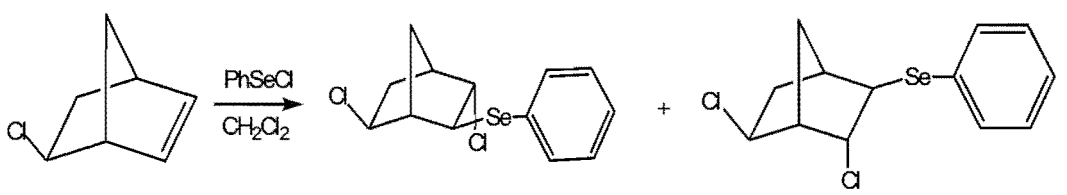
^{13}C NMR (75 MHz, $CDCl_3$),δ 45.04(C1), 65.86(C2), 50.97(C3), 53.78(C4),, 49.62(C5), 35.96(C6),), 33.61(C7), 128.86(C8), 134.61(C9, C13), 129.32(C10, C12), 127.93(C11).

5-*exo*-bromo-3-*endo*-chloro-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.4b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.40(t, 1H J = 1.5, 2.9 Hz, H1), 3.04 (t, 1H J = 2.9, 6.8 Hz, H2n), 4.20 (t, 1H J = 3.9, 8.3 Hz, H3x) 2.79 (t, 1H J = 2.4, 6.8 Hz, H4), 4.64(m, 1H J = 3.9, 4.4, 5.9 Hz, H5n), 2.23 (t, 1H J = 1.5, 4.4 Hz, H6n), 2.22 (t, 1H J = 1.5, 5.9 Hz, H6x), 2.12 (td, 1H J = 1.5, 2.9, 4.4 Hz, H7s), 1.93 (td, 1H J = 1.5, 2.9, 8.3 Hz, H7a), 7.29-7.32 (3H), 7.55-7.60(2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 44.95(C1), 52.61(C2), 65.61(C3), 53.89(C4), 46.09(C5), 43.66(C6), 34.14(C7), 128.55(C8), 134.31(C9, C13), 129.23(C10, C12), 128.19(C11).

6.3(ii) Reactions of 5-e*xo*-chloro-2-norbornene



6.5a **6.5b**

5-*exo*-chloro-2-norbornene (39.7 mg, 0.24 mmol) was dissolved in 1 mL of dichloromethane in a small vial and to this was added 28 mg (0.15 mmol) of phenylselenyl chloride dissolved in 1 mL of the same solvent. The solution was stirred for 20 minutes at room temperature, and then the solvent was removed by

evaporation under reduced pressure at 90 °C. Along with the solvent this removed any unreacted 5-*exo*-chloro-2-norbornene together with any 3-*exo*-chloronortricyclene. ^{1}H NMR analysis showed only (**6.5a**) and (**6.5b**) were present, in a ratio of 52.7:47.3. The products could not be separated by column chromatography.

The same procedure, using excess PhSeCl resulted in the formation of, in addition to (**6.5a**) and (**6.5b**), the corresponding pair of phenyldichloroselanyl derivatives

2-*endo*-5-*exo*-dichloro-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.5a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.55 (m, 1H J = 1.5, 2.5, 4.4 Hz, H1), 4.10 (dt, 1H J = 1.5, 2.0, 4.4 Hz, H2x), 2.95 (dd, 1H J = 2.9, 4.4 Hz, H3n), 2.70 (b, 1H, H4), 3.93 (td, 1H J = 3.4, 3.9, 7.3 Hz, H5n), 2.72(m, 1H J = 2.4, 2.9, 7.3 Hz, H6x), 1.77 (m, 1H J = 1.5, 2.4, 3.9 Hz ,H6n), 2.01 (m, 1H J = 2.9, 4.9, 10.7 Hz, H7s), 1.81 (d, 1H J = 2.4 Hz, H7a), 7.30-7.33(3H), 7.57-7.60(2H).

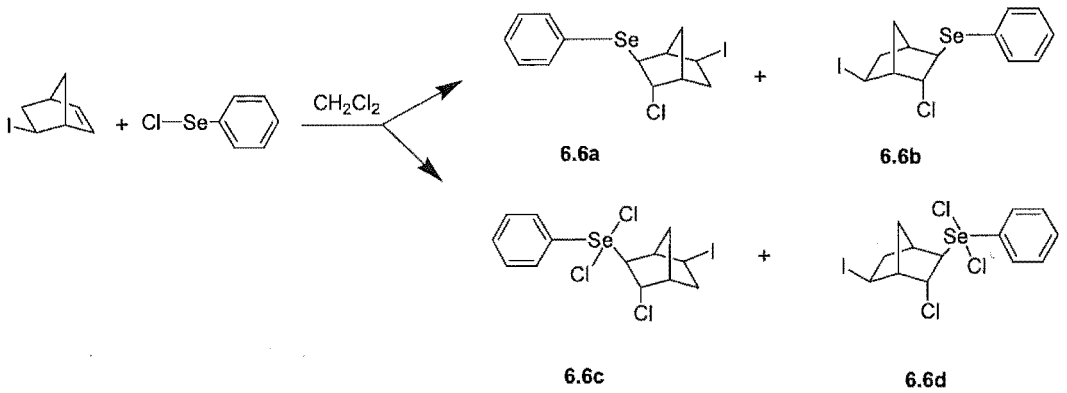
^{13}C NMR (75 MHz, $CDCl_3$),δ 44.50(C1), 65.73(C2), 50.51(C3), 53.37(C4), 59.28(C5), 35.69(C6), 33.14(C7), 134.58(C8), 129.28(C9, C13), 128.53(C10, C12), 128.14(C11).

3-*endo*-5-*exo*-dichloro-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.5b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.42 (d,1H, J = 3.9 Hz, H1), 3.05 (t, 1H J= 3.4 Hz, H2n), 4.20(t, 1H J = 4.4 Hz, H3x), 2.72(dd, 1H J = 2.4, 7.3 Hz, H4), 4.58 (dt, 1H J = 2.4, 2.9, 4.4, 7.3 Hz, H5n), 2.03 (dt, 1H J = 1.5, 3.4, 4.9 Hz, H6x), 2.15 (4d, 1H J = 2.4, 6.8, 7.3 Hz, H6n), 2.04(m, 1H J = 1.5, 3.4.8, 3 Hz, H7s), 1.89 (dt 1H J = 1.5, 3.4, Hz, H7a), 7.31-7.34 (3H), 7.57-7.60 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 44.41(C1), 52.60(C2), 64.95(C3), 53.40(C4), 55.61(C5), 43.31(C6), 33.69(C7), 134.24(C8), 129.20(C9, C13), 128.92(C10, C12), 127.88(C11).

6.3(iii) Reactions of 5-*exo*-iodonorborn-2-ene



5-*exo*-Iodo-2-norbornene (containing 25% 3-iodonortricyclene) (20 mg, 0.09 mmol) was dissolved in 0.5 mL of dichloromethane in small vial. To this 20 mg (0.10 mmol) of phenylselenyl chloride dissolved in 0.5 ml of anhydrous dichloromethane was added and the solution was stirred for 30 minutes at room temperature. The reaction appeared to be rather slow, as judged by the rate of decolourisation of the solution. The solvent was then removed by evaporation under reduced pressure on a hot water bath at 90 °C. ^{1}H NMR analysis of the crude product showed the presence of the four addition products, **6.6a** – **6.6d** present in the ratio 39.7:27.6:18.7:14. This material was put on a silica column and eluted with petroleum ether to give pure samples of (**6.6a**) and (**6.6b**).

Repeating the experiment using an excess of 5-*exo*-iodo-2-norbornene gave (**6.6a**) and (**6.6b**) in a ratio of 58.5:41.5.

2-*endo*-chloro-5-*exo*-iodo-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.6a)

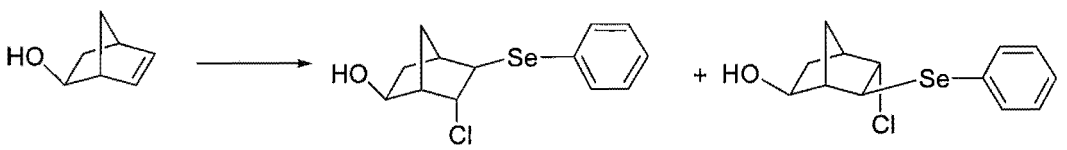
^{1}H NMR (500 MHz, $CDCl_3$), δ 2.44 (td, 1H J = 1.5, 4.4, 5.4 Hz, H1), 4.14 (dd, 1H J = 4.4, 5.9, Hz, H2x), 3.07 (d, 1H J = 4.4 Hz ,H3n), 2.68 (bs, 1H, H4), 3.99 (m, 1H J = 2.0, 2.4, 4.9, 7.8 Hz, H5n), 2.86 (td, 1H J = 2.0, 2.4, 7.8 Hz ,H6x) 2.15 (dd, 1H J = 1.5, 4.9 Hz, H6n), 2.13 (dt, 1H J = 1.5, 2.9 Hz, H7s), 1.90 (dt, 1H J = 1.5, 2.4 Hz, H7a), 7.24 (1H), 7.25 (2H), 7.56 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 45.79(C1), 66.31(C2), 51.34(C3), 54.94(C4), 37.04(C5), 24.40(C6), 34.30(C7), 129.12(C8) 128.08(C9, C13), 129.27(C10, C12), 134.45(C11).

3-*endo*-chloro-5-*exo*-iodo-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.6b)

^{1}H NMR (500 Hz, $CDCl_3$), δ 2.32 (d, 1H J = 2.0 Hz, H1), 3.04 (d, 1H J = 4.4 Hz, H2n), 4.12 (td, 1H J = 4.4, 5.9 Hz, H3x), 2.84(d, 1H J = 2.4 Hz, H4), 4.67(m, 1H J = 2.4, 3.9, 7.8 Hz, H5n), 2.35 (t, 1H J = 4.9, 8.8 Hz, H6x), 2.27 (td, 1H J = 2.4, 2.9, 7.8 Hz, H6n), 2.14 (m, 1H J = 1.5, 2.9 Hz, H7s), 1.99 (m, 1H, H7a).
^{13}C NMR (75 MHz, $CDCl_3$), δ 45.82(C1), 52.75(C2), 66.35(C3), 55.31(C4), 20.3(C5), 44.87(C6), 34.79(C7), 129.30(C8), 127.86(C9, C13), 129.17(C10, C12), 134.25(C11).

6.3(iv) Reaction of 5-*exo*-hydroxynorborn-2-ene



6.7a **6.7b**

5-*exo*-Hydroxy-2-norbornene (20 mg, 018 mmol) was dissolved in 1 mL of dichloromethane. To this 35 mg (0.18 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added dropwise with stirring. The solution was then stirred at room temperature for 20 minutes. The solvent was then removed under reduced pressure on a cold water bath. ^{1}H NMR analysis showed that at least two products were present, one of which still contained a C=C bond. The ratio of the two was 25:75. The mixture was redissolved in dichloromethane, an additional 35 mg (0.18 mmol) of phenylselenyl choride was added, and the solution was stirred for a further 30 minutes. Removal of the solvent under reduced pressure gave a mixture of products that. ^{1}H NMR analysis showed this to be a mixture of (**6.7a**) and (**6.7b**) in a ratio of 90:10. There were also traces of what appeared to be their corresponding phenyldichloroselanyl analogues.

The mixture of products was passed through a dry silica column using as eluent 90:10, petroleum ether:ethyl acetate. The first fraction to emerge was

unreacted phenylselenyl chloride. This was followed by a second fraction consisting of a mixture of (**6.7a**) and (**6.7b**). There was no sign of any product with a phenylselanyl group bonded to the oxygen of the hydroxyl group.

3-*endo*-chloro-5-hydroxy-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.7a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.37 (d, 1H J = 4.4 Hz, H1), 3.05 (t, 1H J = 2.9, 5.9 Hz, H2n), 4.14 (t, 1H J = 4.4, 8.3 Hz, H3x), 2.47 (d, 1H J = 3.9 Hz, H4), 4.50 (d, 1H, J = 6.9 Hz, H5n), 1.90 (ddd,1H J = 2.4, 6.9, 9.3 Hz, H6x), 1.53 (dt, 1H J = 1.5, 2.4, 3.9 Hz, H6n), 1.65 (m, 1H J = 1.5, 2.4, 3.9 Hz, H7a), 1.83 (m, 1H J = 1.5, 2.0, 3.4 Hz, H7s), 7.26-7.29 (3H), 7.55-7.57 (2H).

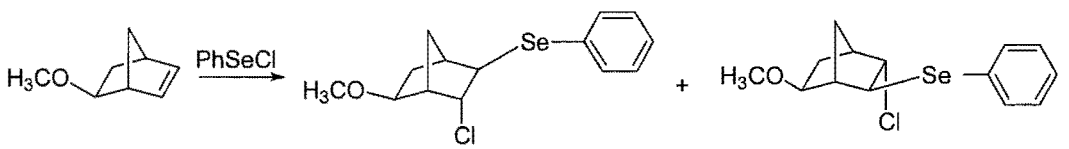
^{13}C NMR (75 MHz, $CDCl_3$),δ 43.64(C1), 53.07(C2), 64.14(C3), 51.81(C4), 68.21(C5), 42.07(C6), 33.01(C7), 129.20(C8), 134.06(C9, C13), 129.14(C10, C12), 127.27(C11).

2-*endo*-chloro-5-hydroxy-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.7b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.43 (dd, 1H J = 2.4, 6.8 Hz, H1), 4.08 (dd, 1H J = 2.4, 5.9 Hz, H2x), 3.87 (d, 1H J = 6.8 Hz, H3n), 2.87 (t, 1H J = 2.9, 7.3 Hz, H4), 4.33 (t, 1H J = 5.9, 6.8 Hz, H5n), 2.14 (m,1H J = 3.9, 6.3, 8.8 Hz, H6x),.1.67 (2H, J = 6.9 Hz,(rest not resolved), H6n), 1.82 (dd, 1H J = 2.0, 2.4 Hz, H7s), 1.32 (dt, 1H J = 2.4, 2.9 Hz, H7a), 7.26-7.29 (3H), 7.53-7.59 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 38.17(C1), 66.25(C2), 52.28(C3), 49.21(C4), 73.28(C5), 34.45(C6), 32.52(C7), 129.20(C8), 134.43(C9, C13), 129.35(C10, C12), 127.91(C11).

6.3(v) Reaction of 5-*exo*-methoxy-2-norbornene



6.8a **6.8b**

5-*exo*-Methoxy-2-norbornene (10 mg, 0.08 mmol) was dissolved in 21 mL of dichloromethane. To this solution phenylselenyl chloride (14.5 mg, 0.08 mmol) dissolved in 1 mL of dichloromethane was added dropwise. The mixture

was stirred for 30 minutes at room temperature. Reaction was comparatively slow. The solvent was then removed under reduced pressure. The ^{1}H NMR of crude product showed that the products of the reaction were (**6.8a**) and (**6.8b**) formed in the ratio 71:29 together with traces of phenyldichloroselanyl compounds. This product was purified by chromatography on dry silica (1:20, compound to silica gel by weight) using as eluent 90:10 petroleum ether:ethyl acetate. The second fraction off the column consisted of a mixture of (**6.8a**) and (**6.8b**).

3-*endo*-chloro-5-*exo*-methoxy-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.8a)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.37 (d, 1H J = 2.4 Hz, H1), 3.06 (dd, 1H J = 2.0, 4.4 Hz, H2n), 4.16 (t, 1H J = 4.4, Hz,H3x), 2.62 (d, 1H J = 4.4 Hz, H4), 3.95 (dd, 1H J = 2.4, 6.8 Hz, H5n), 1.81 (m, 1H J = 1.5, 5.9, 6.3 Hz, H6x), 1.58 (m, 1H J = 2.4, 4.4, 6.9 Hz, H6n), 1.70-1.72 (bs, 2H H7s, 7a), 3.28 (OCH_3),.7.27-7.30 (3H), 7.55-7.57 (2H).

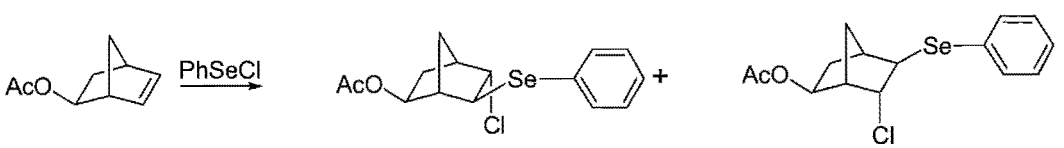
^{13}C NMR (75 MHz, $CDCl_3$),δ 43.43(C1), 53.35(C2), 64.15(C3), 47.99(C4), 77.30(C5), 39.50(C6), 33.47(C7), 56.26(OCH_3), 129.40(C8), 134.02(C9, C13), 129.12(C10, C12),127.62(C11).

2-*endo*-chloro-5-*exo*-methoxy-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.8b)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.34 (d, 1H J = 4.9 Hz, H1), 4.12 (dd, 1H J = 3.9, 5.4 Hz,H2x), 2.87 (q, 1H J = 2.4, 2.9, 3.9 Hz, H3n), 2.45 (d, 1H J = 5.4 Hz, H4), 3.35(d, 1H J = 6.8 Hz, H5n), 2.36(m,1H, H6x) 1.34 (dt, 1H J = 2.4, 4.9 Hz, H6n), 1.74 (t, 1H J = 1.5, 4.0 Hz, H7a), 1.63 (m, 1H H7s), 3.29 (s,OCH_3), 7.24-7.26 (3H), 7.58-7.7.60 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 43.22(C1), 66.90(C2), 49.28(C3), 48.13(C4), 82.33(C5), 31.85(C6), 32.88(C7), 56.15(OCH_3), 129.40(C8), 134.29(C9, C13), 131.43(C10, C12), 127.78(C11).

6.3(vi) Reaction of 5-*exo*-acetoxy-2-norbornene



6.9a **6.9b**

5-*exo*-Acetoxy-2-norbornene (8 mg, 0.06 mmol) was dissolved in 0.5 mL of dichloromethane in a 5 ml vial. To this 13 mg (0.07 mmol) of phenylselenyl chloride dissolved in 0.5 mL of dichloromethane was added dropwise. The yellow colour disappeared rapidly, showing that addition was fast. The mixture was stirred for 10 minutes at room temperature, and the solvent was then removed under reduced pressure. ^{1}H NMR analysis showed the presence of the two adducts, (**6.9a**) and (**6.9b**) in a ratio of 53:47. There appeared to be no other products present, so the mixture was not chromatographed.

5-*exo*-acetoxy-2-*endo*-chloro-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.9a)

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.51 (m, 1H, H1), 4.09 (t, 1H J = 2.9, 4.4 Hz, H2x), 2.99 (t, 1H J = 2.9, 6.3 Hz, H3n), 2.43 (s, 1H, H4), 4.70 (d, 1H J = 6.3 Hz, H5n), 2.54 (dd, 1H J = 2.0,7.3 Hz, H6x), 1.44 (dt, 1H J = 2.8, 4.4 Hz, H6n), 1.72 (m, 1H, H7a), 1.74 (m, 1H J = 2.0, 4.0 Hz, H7s), 2.01 (OCH_3), 7.26-7.30(3H), 7.56-7.57(2H).

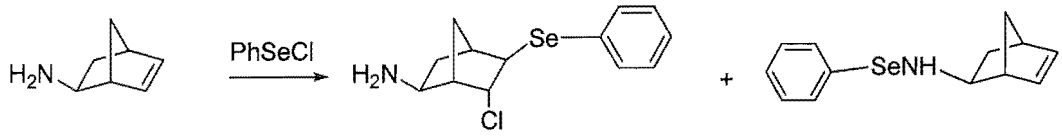
^{13}C NMR (75 MHz, $CDCl_3$) δ, 43.58(C1), 65.94(C2), 48.53(C3), 49.39(C4), 75.18(C5), 32.04(C6), 33.27(C7), 169.36(CO), 21.17(CH_3), 128.88(C8), 133.98(C9, C13), 129.24(C10, C12), 127.82(C11).

5-*exo*-acetoxy-3-*endo*-chloro-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.9b)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.39 (d, 1H J = 3.9 Hz, H1), 3.09 (t, 1H J = 2.9, 5.9 Hz, H2n), 4.15 (t, 1H J = 3.9, 4.4 Hz, H3x), 2.65 (d, 1H J = 3.9 Hz, H4), 5.29 (d, 1H J = 6.3 Hz, H5n), 2.03 (t, 1H J = 2.8, 4.8 Hz, H6x), 1.64 (m, 1H J = 2.4, 4.0 Hz, H6n), 1.80 (m, 1H, H7s), 1.76 (dd, 1H J = 2.0, 4.0 Hz, H7a), 2.01 (CH_3), 7.26-7.30 (3H), 7.56-7.57 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 43.69(C1), 52.93(C2), 63.54(C3), 49.20(C4), 71.79(C5) 40.03(C6), 33.94(C7), 170.33(CO), 21.21(CH_3), 129.14(C8), 134.12(C9, C13), 129.21(C10, C12), 127.79(C11).

6.3(vii) Reactions of 5-*exo*-amino-2-norbornene



6.10a **6.10b**

5-*exo*-Amino-2-norbornene (19 mg, 17.4 mmol) was dissolved in 1 mL of dichloromethane in a 5 ml vial. To this solution 37 mg (19.3 mmol) of phenylselenyl chloride dissolved in 1 mL of anhydrous dichloromethane was added dropwise with stirring. Stirring was continued for 15 minutes at room temperature. The solvent was then removed under reduced pressure. The ^{1}H NMR of the crude product was then taken and showed there were two compounds present in a ratio of 33:67. One was the adduct (**6.10a**). The other contained a C=C bond and was identified from its NMR spectrum as (**6.10b**). Stirring for 60 minutes gave the same two products, but this time the ratio of (**6.10a**) to (**6.10b**) was 80:20. .The NMR spectra consisted of broad singlets and the coupling constants were difficult to resolve. The impure mixture was columned on silica, eluting with different solvents, (a) various ratios of petroleum ether and ether, (b) pure dichloromethane and (c) methanol. The same impure material eluted with methanol; the other solvents failed to remove the product from the column. Chromatography on alumina was also unsuccessful. The proton spectrum of the adduct was not good enough for coupling constants to be determined.

5-*exo*-amino-3-*endo*-chloro-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.10a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.78 (1H, H1), 2.97(1H, H2), 4.15 (1H, H3), 3.14 (1H, H4), 2.66 (1H, H5n), 1.98 (1H, H6), 1.85 (1H, H6), 1.72 (1H, H7), 1.66 (1H, H7).7.22-7.30 (3H), 7.55-7.60 (2H).

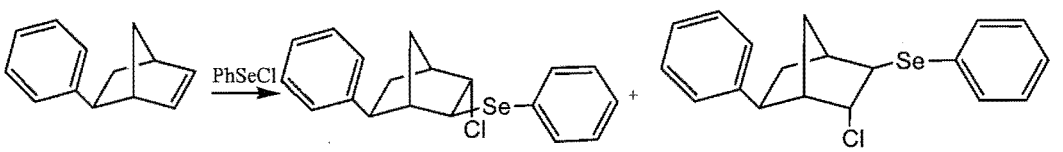
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.19(C1), 51.39(C2), 65.68(C3), 45.47(C4), 46.23(C5), 41.52(C6), 32.71(C7), 129.15(C8), 134.26(C9, C13), 131.45(C10, C12), 127.73(C11).

5-*exo*-phenylselanylamino-2-norbornene (6.10b)

^{1}H NMR (500 MHz, $CDCl_3$),δ 3.29 (1H, H1), 6.02 (1H, H2), 6.20(1H, H3), 3.02 (1H, H4), 3.94(1H, H5n), 2.86(1H, H6x), (1H), 2.58 (1H, H6n), 2.21 (1H, H7), 1.90 (1H, H7), 7.26-7.30(3H), 7.55-7.61 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ, 50.29(C1), 133.47(C2), 139.79(C3), 48.41(C4), 52.93(C5), 33.38(C6), 30.11(C7), 129.17(C8), 134.20(C9, C13), 130.86(C10, C12), 127.68.(C11)..

6.3(viii) Reaction of 5-*exo*-phenyl-2-norbornene



6.11a 6.11b

5-*exo*-Phenyl-2-norbornene (10 mg, 0.06 mmol) was dissolved in 0.5 mL of dichloromethane in a 5 mL vial. To this 11.4 mg (0.06 mmol) of phenylselenyl chloride dissolved in 0.5 mL of dichloromethane was added dropwise. The addition reaction proceeded quite rapidly. The solution was stirred for 20 minutes at room temperature and the solvent was then removed under reduced presssure. The ^{1}H NMR of the product showed the presence of (**6.11a**) and (**6.11b**) (in 75:25 ratio) along with traces of its phenyldichloroselanyl analogues. Passing the crude product through a silica column (1:20) and eluting with 90:10 pentane:ether gave a mixture of pure (**6.11a**) and (**6.11b**).

2-*endo*-chloro-5-*exo*-phenyl-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.11a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.60 (s, 1H, H1), 4.21(d, 1H J = 4.4 Hz, H2x), 3.32 (t, 1H J = 2.4, 5.4 Hz, H3n), 2.53 (d, 1H J = 1.5 Hz, H4), 2.94 (dd, 1H J = 5.4, 5.9 Hz, H5n), 2.57 (d, 1H J = 3.4 Hz, H6x), 1.69 (dd, 1H J =3.9, 5.4 Hz, H6n), 1.74 (s,1H, H7s), 1.66 (t, 1H J = 4.4 Hz, H7a), 7.23-7.30 (6H), 7.58-7.60 (4H).

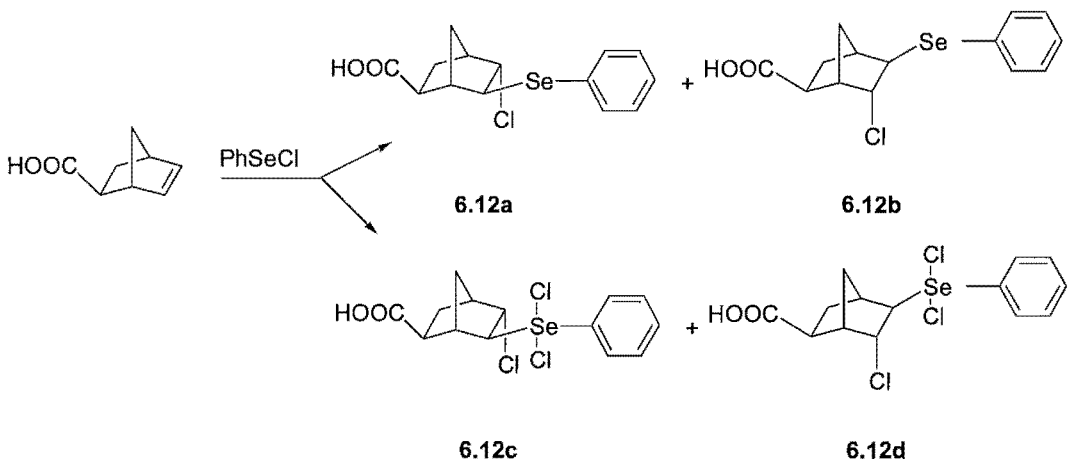
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.83(C1), 67.30(C2), 54.82(C3), 50.50(C4), 46.99(C5), 30.91(C6), 34.22(C7), 129.41(C8), 133.85(C9, C13), 129.48(C10, C12), 127.60(C11), 145.23(C8') 128.63(C9', C13'), 127.79(C10', C12'), 125.99(C11').

3-*endo*-chloro-5-*exo*-phenyl-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.11b)

^1H NMR (500 MHz, $CDCl_3$),δ 2.47 (s, 1H, H1), 3.20 (d, 1H J = 3.4 Hz, H2n), 4.25 (t, 1H J = 1.5, 4.9 Hz, H3x), 2.57(d, 1H J = 3.4 Hz, H4), 3.61 (t, 1H J = 7.3 Hz, H5n), 1.92 (d, 1H J = 3.9 Hz, H6x), 1.91 (d, 1H J = 2.4 Hz, H6n), 1.76 (d, 1H J = 1.5 Hz, H7s), 1.71 (t, 1H J = 1.5, 5.9 Hz, H7a), 7.16-7.22 (6H), 7.58-7.62 (4H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 38.29(C1), 53.48(C2), 67.53(C3), 45.11(C4), 51.06(C5), 38.19(C6), 34.01(C7), 128.69(C8), 134.17(C9, C13), 129.51(C10, C12), 127.08(C11), 145.13(C8'), 127.64 (C9',C13'), 127.28(C10', C12'), 126.26(C11).

6.3(ix) Reactions of 5-*exo*-carboxy-2-norbornene



Norborn-5-ene-2-*exo*-carboxylic acid (23.7 mg, 0.17 mmol) was dissolved in 1 mL of dichloromethane in a 5 mL vial. To this 33.0 mg (0.17 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added dropwise with stirring. Stirring was continued for 20 minutes at room temperature.

Evaporation of the solvent under reduced pressure and analysis of the product by ^{1}H NMR showed it consisted of (**6.12a**) and (**6.12b**) present in the ratio 68.6% to 31.4%.

When the reaction was repeated with excess phenylselenyl chloride present the product was found to contain in addition to (**6.12a**) and (**6.12b**) the two corresponding phenyldichloroselanyl adducts (**6.12c**) and (**6.12d**)with the ratio (**6.12a**):(**6.12b**):(**6.12c**):(**6.12d**) being 55.7:23.0:11.8:9.5. When excess of norborn-5-ene-2-*exo*-carboxylic acid was used only (**6.12a**) and (**6.12b**) were formed. Pure samples of (**6.12a**) and (**6.12b**) were obtained by chromatography on silica. Using 80:20 petroleum ether:ethyl acetate as eluent any phenyselenyl chloride present came off the column first. Subsequent elution with ethyl acetate gave (**6.12a**) and (**6.12b**).

2-*endo*-chloro-5-*exo*-carboxy-3-*exo*-phenylselanyl[2.2.1]bicycloheptane(6.12a)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.53 (d, 1H J = 4.4 Hz, H1), 4.16 (t, 1H J = 3.9 Hz, H2x), 3.13 (t, 1H J = 2.9, 5.4 Hz, H3n), 2.66 (s, 1H, H4), 2.52 (d, 1H J = 5.4 Hz, H5n), 2.31 (t, 1H J = 10.7, 11.7 Hz, H6x), 1.85 (t, 1H J = 4.9, 9.8 Hz, H6n), 1.71 (dd, 1H J = 1.5, 11.2 Hz, H7s), 1.82 (dd, 1H J = 3.9, 8.3 Hz, H7a), 7.24-7.30 (3H), 7.56-7.60(2H).

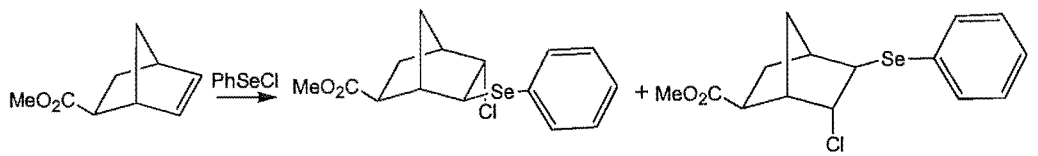
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.04(C1), 66.59(C2), 53.41(C3), 47.91(C4), 45.97(C5), 26.40(C6), 34.67(C7), 180.43(COOH), 128.93(C8), 134.20(C9, C13), 129.25(C10, C12), 127.89(C11).

3-*endo*-chloro-5-*exo*-carboxy-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.12b)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.40 (d, 1H J = 3.9 Hz, H1), 3.08 (t, 1H J = 3.4, 6.3 Hz, H2n), 4.19 (t, 1H J = 4.4 Hz, H3x), 2.80 (d, 1H J = 3.9 Hz, H4), 3.20 (dd, 1H J = 5.4, 9.8 Hz, H5n), 2.04 (dt, 1H J = 4.4, 9.8 Hz, H6x), 1.73 (t, 1H J = 9.8 Hz, H6n), 1.64 (dd, 1H J = 1.5, 11.2, H7s), 1.83 (d, 1H J = 2.0 Hz, H7a), 7.24-7.30 (3H), 7.56-7.60 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 44.10(C1), 53.02(C2), 66.14(C3), 48.28(C4), 38.84(C5), 33.99(C6), 34.72(C7), 181.41(COOH), 128.10(C8), 134.23(C9, C13), 129.20(C10, C12), 127.82(C11).

6.3(x) Reaction of 5-*exo*-methoxycarbonyl-2-norbornene



6.13a **6.13b**

5-*Exo*-carbomethoxy-2-norbornene (21.5 mg, 014 mmol) was dissolved in 1 mL of dichloromethane. To this solution 28 mg (0.146 mmol) of phenylselenyl chloride dissolved in 1 mL of the same solvent was added dropwise. The reaction was fast at first and then slowed down later. After the addition was complete the solution was then stirred for 10 minutes at room temperature and the solvent then removed under reduced pressure. The crude product was analysed by ^{1}H NMR. This showed that the two addition products (**6.13a**) and (**6.13b**) had been formed in a ratio of 69.4:30.6. The crude product was purified by passing through a silica column using as eluent 90:10, petroleum ether:ethyl acetate. Some unreacted phenylselenyl chloride was eluted. The column was then eluted with pure ether, and the two addition products came off the column.

2-*endo*-chloro-5-*exo*-methoxycarbonyl-3-*exo*-phenylselanyl[2.2.1] bicycloheptane (6.13a)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.54 (bd, 1H, H1), 4.17 (dd, IH J = 3.9, 5.9 Hz, H2x), 3.13(dd, 1H J = 4.0, 5.2 Hz, H3n), 2.64(s, 1H, H4), 2.51 (dd, 1H J = 5.9, 9.1 Hz, H5n) 2.29 (dt, 1H J = 3.9, 6.3 Hz,H6x), 1.84 (m, 1H J = 1.5, 3.2, 5.9 Hz, H6n), 1.71 (t, 1H J = 1.6, 2.8 Hz, H7s), 1.78 (m, 1H J = 1.6, 3.2 Hz, H7a), 3.67 (OCH_3). 7.26-7.32 (3H), 756-7.60 (2H).

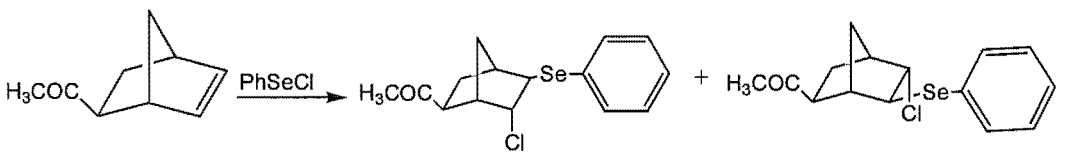
^{13}C NMR (75 MHz, $CDCl_3$),δ 44.05(C1), 66.86(C2), 53.51(C3), 47.98(C4), 45.97(C5), 26.48(C6), 34.65(C7), 51.95(OCH_3), 174.73(CO), 129.17(C8), 134.16(C9, C13), 129.21(C10, C12), 127.80(C11).

3-*endo*-chloro-5-*exo*-methoxycarbonyl-2-*exo*-phenylselanyl[2.2.1] bicycloheptane (6.13b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 3.17 (dd, 1H J = 5.2, 9.2 Hz, H1), 3.08 (t, 1H J = 1.2, 4.0 Hz, H2n), 4.19 (t, 1H J = 2.0, 6.7 Hz, H3x), 2.76 (dd, 1H J = 2.8, 6.7 Hz, H4), 2.40 (bd, 1H J = 3.6 Hz, H5n), 2.05 (dt, 1H J = 5.2, 9.2 Hz, H6x), 1.64 (td, 1H J = 1.6, 2.7, 8.3 Hz, H6n), 1.69 (m, 1H J = 1.6, 2.0, 3.6 Hz, H7s), 1.80 (m, 1H J = 1.2, 2.8, 4.8 Hz, H7a), 3.69 (OCH_3), 7.26-7.32 (3H), 7.56-7.60 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 38.65(C1), 53.13(C2), 66.37(C3), 48.40(C4), 44.12(C5), 34.04(C6), 34.60(C7), 51.98(OCH_3), 175.62(CO), 129.12(C8), 134.18(C9, C13), 129.17(C10, C12), 127.76(C11).

6.3(xi) Reaction of 5-*exo*-acetyl-2-norbornene



6.14a **6.14b**

5-*exo*-Acetyl-2-norbornene (15 mg, 0.11 mmol) was dissolved in 0.5 mL of dichloromethane in a 5 mL vial. To this 21.1 mg (0.11 mmol) of phenylselenyl chloride dissolved in 0.5 mL of dichloromethane was added drop-wise and the solution stirred at room temperature for 20 minutes. Based on the rate of decolourisation of phenylselenyl chloride solution, the reaction appeared to be very fast. The solvent was removed by evaporation under reduced pressure. The ^{1}H NMR of the product was determined and this showed the presence of the two addition products, (**6.14a**) and (**6.14b**) in the ratio 35.8:64.2. This material was further purified by passing through a silica column (1:20), eluting first with petroleum ether to remove traces of unreacted phenylselenyl chloride, and finally with 90:10, petroleum ether: ethyl acetate to obtain the two addition products.

5-*exo*-acetyl-3-*endo*-chloro-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.14a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.50 (s, 1H, H1), 3.17 (t, 1H J = 3.4, 5.9 Hz, H2n), 4.18 (dt, 1H J = 3.9, 5.9, 8.3 Hz, H3x), 2.56 (s, 1H, H4), 2.58 (dd, 1H J = 3.4, 6.3 Hz, H5n), 2.17 (m, 1H J = 2.4, 2.9, 9.3 Hz, H6x), 1.81 (m, 1H J = 1.5, 2.4, 5.9 Hz, H6n), 1.49 (dt, 1H J = 1.5, 7.8 Hz, H7a), 1.72 (m, 1H J = 1.5, 2.4, 7.8 Hz, H7s), 2.17 (CH_3), 7.28-7.32 (3H), 7.56-7.60 (2H)

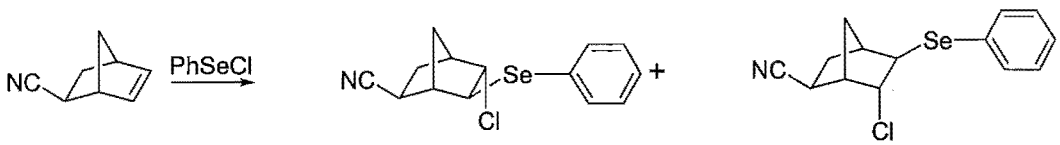
^{13}C NMR (75 MHz, $CDCl_3$),δ 44.19(C1), 53.95(C2), 66.94(C3), 46.78(C4), 54.12(C5), 25.03(C6), 34.24(C7), 207.71(CO), 28.71(CH_3), 129.19(C8), 134.22(C9, C13), 129.23(C10, C12),127.85(C11).

5-*exo*-acetyl-2-*endo*-chloro-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.14b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.69 (dd, 1H J = 1.5, 3.9 Hz, H1), 4.21 (t, 1H J = 4.4, 8.3 Hz, H2x), 3.09 (dd, 1H J = 2.9, 6.8 Hz, H3n), 2.39 (d, 1H J = 3.4 Hz, H4), 3.23 (dd, 1H J = 5.4, 8.3 Hz, H5n), 2.04 (dt, 1H J = 4.9, 12.2 Hz, H6x), 1.54 (dd, 1H J = 2.9, 12.2 Hz, H6n), 1.44.(dt, 1H J = 1.5, 2.0 Hz, H7a), 1.70 (dd, 1H J = 1.5, 3.9 Hz, H7s), 2.18 (CH_3), 7.28-7.32 (3H), 7.5-7.60 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 47.45(C1), 66.61(C2), 53.23(C3), 44.26(C4), 46.61(C5), 32.35(C6), 34.12(C7), 208.79(CO), 28.63(CH_3), 129.12(C8), 134.20(C9, C13), 129.19(C10, C12), 127.76(C11).

6.3(xii) Reaction of 5-*exo*-cyano-2-norbornene



6.15a **6.15b**

5-*exo*-Cyano-2-norbornene (20 mg, 0.17 mmol) was dissolved in 1 mL of dichloromethane. To this was added 20 mg (0.10 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane. The solution was stirred for stirred for 30 minutes at room temperature, and the solvent then removed under reduced pressure. The ^{1}H NMR of the crude product showed the presence of (**6.15a**) and

(**6.15b**) in a ratio of 47:53 together with some unreacted 6-*exo*-cyano-2-norbornene. The product was purified by passing through a dry silica column (1:20) using eluent 80:20, petroleum ether:ether. The first fraction consisted of unreacted 6-*exo*-cyano-2-norbornene and the second a mixture of the two addition products.

When the experiment was repeated under same conditions, but with excess phenylselenyl chloride present, four addition products were obtained in a ratio of 31:47:13:9. These were (respectively) (**6.15a**), (**6.15b**), and their two corresponding phenyldichloroselanyl analogues.

2-*endo*-chloro-5-*exo*-cyano-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (5.15a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.63(s, 1H, H1), 4.11(td,1 H J = 1.5, 2.0, 6.8 Hz, H2x), 2.98 (t, 1H J = 2.9, 6.8 Hz, H3n), 2.58 (d, 1H, J = 3.9 Hz, H4), 2.47 (t, 1H J = 1.0, 1.5 Hz, H5x), 2.48(t, 1H, J = 1.5, 2.4 Hz, H6x), 1.77(td, 1H J = 1.5, 3.9, 5.9, Hz, H6n), 1.80 (m, 1H J = 1.5, 2.9 Hz, H7s), 1.93 (1H, H7a),7.30-7.32 (3H), 7.55-7.56(2H).

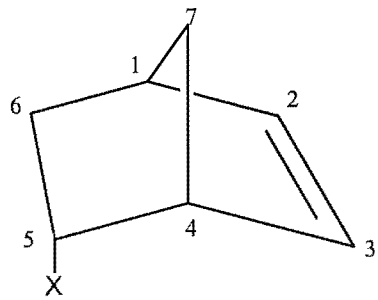
^{13}C NMR (75 MHz, $CDCl_3$), δ 48.47(C1), 65.36(C2), 51.87(C3), 44.41(C4), 30.79(C5), 28.27(C6), 34.86(C7), 129.66(C8), 134.60(C9, C13), 129.30(C10, C12), 128.28(C11).

3-*endo*-chloro-5-*exo*-cyano-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.15b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.79 (d, 1H J = 3.9 Hz, H1), 4.17 (t, 1H J = 3.9, 4.4 Hz, H2x), 3.03 (t, 1H J = 3.4 Hz, H3n), 2.45 (t, 1H J = 2.0, 2.4 Hz, H4), 1.99 (m, 1H J = 2.4, 4.9 Hz, H6x), 1.86 (m, 1H J = 2.0, 2.4, 3.9 Hz, H6n), 3.23 (dd, 1H J = 4.4, 4.9 Hz, H5n), 1.83 (t,1H J = 1.0, 2.9 Hz, H7s), 1.96 (d, 1H J = 4.4 Hz, H7a), 7.30-7.33 (3H), 7.55-7.56 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 49.16(C1), 52.03(C2), 65.04(C3), 43.68(C4), 24.57(C5), 35.69(C6), 35.11(C7), 129.30(C8), 134.35(C9, C13), 129.05(C10, C12) 128.02(C11).

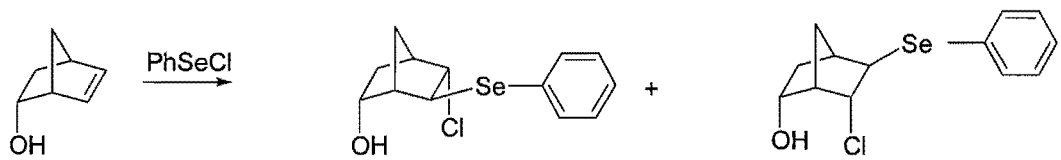
6.4 Reactions of 5-*endo*-X-substituted-2-norbornenes with phenylselenyl chloride



The range of 5-X-*endo*-substituted-2-norbornenes covered was more restricted than in the *exo*-series, the most notable absentees being X = Cl, Br, I. The reasons for their omission have been discussed previously.

The basic method used in the reactions of the *endo* alkenes was the same as that used for the *exo* series of compounds. Steric hindrance by the *endo* substituent tended to lead to yields of the 2-chloro-3-phenylselanyl adducts usually being either low, in some case, negligible.

6.4(i) Reactions of 5-*endo*-hydroxy-2-norbornene



6.16a **6.16b**

5-*endo*-Hydroxy-2-norbornene (25 mg, 023 mmol) was dissolved in 1 mL of dichloromethane. To this 20 mg (010 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added dropwise and the mixture and stirred for 20 minutes at room temperature. The solvent was then removed under reduced pressure. ^{1}H NMR analysis of the product established the presence the two selenium addition products (**6.16a**) and (**6.16b**), formed in a ratio of 69:31, together with some unreacted 5-*endo*-hydroxy-2-norbornene. The product was

purified by passing through a dry silica column (1:30) using eluent 90:10, petroleum ether:ethyl acetate. The only fraction to emerge was unreacted starting material. Subsequent elution with ethyl acetate alone gave the two adducts.

2-*endo*-chloro-5-*endo*-hydroxy-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.16a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.40 (d, 1H J = 3.9 Hz, H1), 4.27 (dd, 1H J = 2.9, 4.4 Hz, H2x), 3.90 (dd, 2.9, 4.0 Hz, H3n), 2.39(s, H4), 4.31 (t, 1H, J= 3.9, 5.4 Hz,H5x), 1.89 (td, 1H J = 2.9, 3.9, .9 Hz, H6x), 1.73 (t, 1H J = 3.4 Hz, H6n), 1.78 (d, 1H J = 11.2 Hz, H7a), 1.52 (1H J = 11.2 Hz, H7s), 7.27-7.31 (3H), 7.57-7.62 (2H).

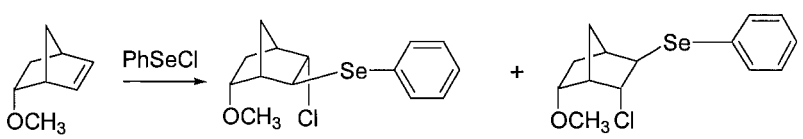
^{13}C NMR (75 MHz, $CDCl_3$), δ 45.27(C1), 68.05(C2), 44.59(C3), 50.67(C4), 72.24(C5), 31.14(C6), 35.32(C7), 127.88(C8), 133.55(C9, C13), 129.10(C10, C12), 127.40(C11).

3-*endo*--chloro-5-*endo*-hydroxy-2-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.16b)

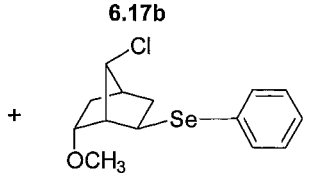
^{1}H NMR (500 MHz, $CDCl_3$) δ 2.38 (s, 1H, H1), 3.45 (t, 1H J = 3.4, 7.3 Hz, H2n), 4.34 (t, 1H J = 3.9, 5.4 Hz, H3x), 2.64 (bs, 1H, H4), 4.36 (t, 1H J = 3.9, 5.4 Hz, H5x),1.73 (t, 1H J = 3.4, 7.3 Hz, H6x), 1.45 (bd, 11.2 Hz, H6n), 2.37 (s, 1H, H7a), 1.24 (t, 1H J = 4.4, 12.2 Hz, H7s), 7.27-7.31 (3H), 7.57-7.62 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 44.39(C1), 54.49(C2), 66.42(C3), 47.31(C4), 74.99(C5), 35.43(C6), 40.29(C7), 127.67(C8), 134.35(C9, C13), 129.20(C10, C12), 127.67(C11).

6.4(ii) Reaction of 5-*Endo*-methoxy-2-norbornene



6.17a **6.17b**



6.17c

5-*endo*-Methoxy-2-norbornene (10 mg, 0.08 mmol) was dissolved in 0.5 mL of dichloromethane in a 5 mL vial. To this 18.5 mg (0.09 mmol) of phenylselenyl chloride dissolved in 0.5 mL of dichloromethane was added dropwise and the solution was stirred at room temperature for 20 minutes. Decolourisation of the reagent was very rapid indicating that addition reaction was fast. The solvent was removed under reduced pressure. ^{1}H NMR of the crude sample showed that apparently three addition products were present. The two expected adducts, (**6.17a**) and (**6.17b**), were identified. The third was assigned the structure (**6.17c**). The (**6.17a**) (**6.17b**):(**6.17c**) ratio was 78.4:7.2:14.4. The mixture was passed through a dry silica column (1:50) using eluent 90:10 petroleum ether:ether as eluent. The only fraction to emerge was a mixture of the three addition products. Because (**6.17c**) was present in relatively low yield, and could not be separated from the other two components, the assignment of the structure above must be regarded as extremely tentative.

2-*endo*-chloro-5-*endo*-methoxy-3-*exo*-phenyselanyl[2.2.1]bicycloheptane (6.17a)

^{1}H NMR (500 MHz,$CDCl_3$), δ, 2.40(bs, 1H, H1), 4.21 (t, 1H J = 3.4, 7.8 Hz, H2x), 3.70 (dd, 1H J = 2.9, 4.9 Hz, H3n), 2.53 (t, 1H J = 2.4, 3.9 Hz ,H4) 3.77 (m, 1H J = 3.9, 4.9, 9.3 Hz, H5x), 1.79 (t, 1H J =3.4, 7.8 Hz, H6x), 1.43 (dd, 1H J = 3.4, 7.3 Hz, H6n), 1.50 (t, 1H J = 1.0, 2.4 Hz, H7s), 1.81 (dd, 1H J = 1.5, 4.4 Hz, H7a), 3.10 (s, OCH_3). 7.27-7.29 (3H), 7.61-7.63 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 44.79(C1), 67.83(C2), 45.03(C3), 47.44(C4), 81.28(C5), 34.97(C6), 28.63(C7), 56.78(OCH_3), 129.15(C8), 134.40(C9, C13), 129.06(C10, C12), 127.68(C11).

3-*endo*-chloro-5-*endo*-methoxy-2-*exo*-phenyselanyl[2.2.1]bicycloheptane (6.17b)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.45(s1H, H1), 2.72 (bd, 1H, H2n), 4.37 (dd, 1H J = 2.0, 3.9 Hz, H3x), 3.39 (s, 1H, H4), 3.83 (d, 1H J =3.9 Hz H5x), 2.17 (m, 1H J =4.9, 5.9 Hz, H6x), 1.22 (t, 1H J = 3.9, 7.5 Hz, H6n), 1.85(t, 1H J = 1.2, 3.6 Hz, H7s), 1.61 (t, 1H J = 3.4, 7.3 Hz, H7a), 3.31 (OCH_3), 7.26-7.27 (3H), 7.60-7.61 (2H).

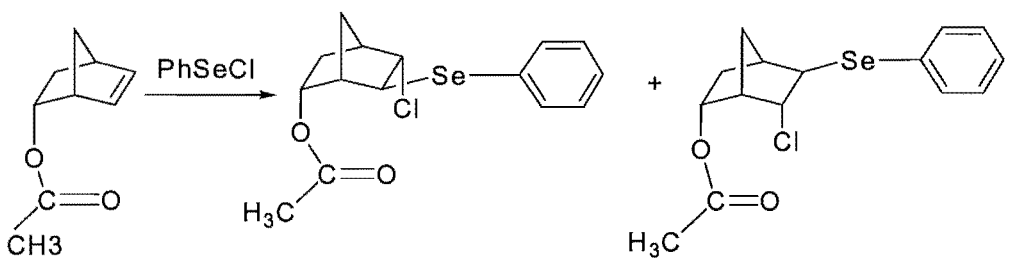
^{13}C NMR (75 MHz, $CDCl_3$),δ 43.28(C1), 57.23(C2), 62.10(C3), 50.21(C4), 80.34(C5), 34.94(C6), 31.15(C7), 57.72(OCH_3), 129.02(C8), 133.83(C9, C13), 129.25(C10, C12), 127.31(C11).

7-chloro-6-*endo*-methoxy-2-*exo*-phenyselanyl[2.2.1]bicycloheptane (6.18c)

^1H NMR (500 MHz, $CDCl_3$),δ 2.46 (d,1H J = 6.3 Hz, H1), 1.53 (t, 1H J = 1.5, 2.9 Hz, H2n), 2.91 (m, 1H, H2x), 0.96 (t, 1H J = 2.0, 3.4 Hz,H3x), 3.60 (t, 1H J = 3.9 Hz, H4), 3.85 (d, 1H J = 2.8 Hz, H5x), 1.91 (dd, 1H J = 2.0, 3.4 Hz, H6x), 1.41 (d,1H J = 2.0 Hz, H6n), 4.30 (t, 1H J = 2.4, 4.9 Hz, 1H7s), 7.24-7.25 (3H),7.68-7.70 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 46.73(C1), 45.66(C2), 29.66(C3), 53.09(C4), 81.68(C5), 35.06(C6), 72.08(C7), 57.89(OCH_3), 128.79(C8), 133.27(C9, C13), 131.45(C10, C12), 126.93(C11).

6.4(iii) Reaction of 5-*endo*-acetoxy-2-norbornene



6.18a **6.18b**

5-*endo*-Acetoxy-2-norbornene (40 mg, 28 mmol) was dissolved in 1 mL of dichloromethane. To this solution phenylselenyl chloride (60 mg, 0.31 mmol) dissolved in 1 mL of dichloromethane was added dropwise with stirring. The mixture was then stirred for 20 minutes at room temperature, after which time the solvent was removed under reduced pressure. ^1H NMR analysis of the crude product showed the presence of (**6.18a**) and (**6.18b**) in the ratio of 66.5:33.5, together with traces of their phenyldichloroselanyl analogues. This material was further purified by passing through a dry silica column (1:30, ratio of compound to silica gel by weight). Elution with 80:20, petroleum ether:ethyl acetate gave as the first fraction a mixture of pure (**6.18a**) and (**6.18b**).

5-*endo*-acetoxy-2-*endo*-chloro-3-*exo*-phenyselanyl[2.2.1]bicycloheptane (6.18a)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.45 (d, 1H J = 3.9 Hz, H1), 4.23 (dt, 1H J = 4.4, 5.9 Hz, H2x), 3.68 (t, 1H J = 2.9, 4.9 Hz, H3n), 2.60 (t, 1H J = 3.4, 4.4 Hz, H4), 5.03 (dt, 1H J = 3.9, 8.3 Hz, H5x), 1.98 (m, 1H J = 5.9, 7.8, 11.2 Hz, H6x), 1.86 (dt, 1H J = 3.5, 3.9, 6.3 Hz, H6n), 1.80 (dt, 1H,J = 1.5, 3.4 Hz, H7a), 1.58 (dd, 1H J = 1.5, 8.3 Hz, H7s), 2.03 (s, CH_3), 7.27-7.30 (3H), 7.54-7.57 (2H).

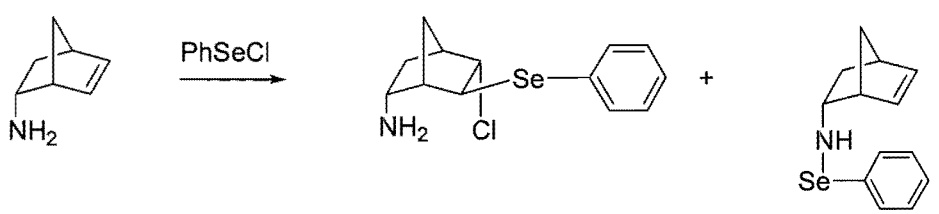
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.61(C1), 67.11(C2), 45.19(C3), 48.37(C4), 74.45(C5), 28.39(C6), 34.73(C7), 170.73(CO), 20.95(CH_3), 129.37(C8), 133.52(C9, C13), 129.10(C10, 12), 127.56(C11).

5-*endo*-acetoxy-3-*endo*-chloro-2-*exo*-phenyselanyl[2.2.1]bicycloheptane (6.18b)

^{1}H NMR (500 MHz,$CDCl_3$), δ 2.59 (bs, 1H, H1), 3.01(t, 1H J = 2.9, 4.4 Hz, H2n), 4.17 (t, 1H J = 4.9, 7.3 Hz, H3x), 2.87 (dd, 1H J = 2.9, 4.9 Hz, H4), 5.21 (dd, 1H J = 2.9, 5.4 Hz, H5x), 2.28 (dd, 1H J = 4.4, 4.9 Hz, H6x), 1.75 (dd, 1H J = 3.9, 10.7 Hz, H6n), 1.02 (dt, 1H J = 3.4, 6.3 Hz, H7s), 1.33 (dd, 1H J = 1.5, 11.2 Hz, H7a), 2.02 (s, CH_3), 7.26-7.30 (3H), 7.53-7.56 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 43.53(C1), 52.88(C2), 65.88(C3), 49.15(C4), 71.74(C5), 29.63(C6), 33.90(C7), 169.51(CO), 21.17(CH_3), 129.19(C8) 134.07(C9, C13), 129.20(C10, C12), 127.77(C11).

6.4(iv) Reaction of 5-*endo*-amino-2-norbornene



6.19 a **6.19b**

5-*endo*-Amino-2-norbornene (20 mg, 17.4 mmol) was dissolved in 1 mL of dichloromethane. To this, 38 mg (19.3 mmol) of phenylselenyl chloride

dissolved in 1 mL of dichloromethane was added dropwise and the solution was stirred at room temperature for 30 minutes. The solvent was then removed under reduced pressure. The ^{1}H NMR of the crude mixture was taken and showed the presence of two products present in a ratio of 90:10. The major product was one of the two expected adducts, (**6.19a**). The other product, (**6.19b**), was that resulting from the attack of the phenylselenyl chloride on the amino group. The ^{1}H NMR spectra were broad and the coupling constants were not well defined.

5-*endo*-amino-2-*endo*-chloro-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.19a)

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.43(1H, H1), 4.26 (1H, H2), 4.04 (1H, H3), 3.76 (1H, H4), 2.76 (1H, H5x), 2.02 (1H, H6x), 1.99 (1H, H6n), 1.79 (d,1H, H7s), 1.57 (d,1H, H7a), 7.21 7.28 (3H), 7.59-7.65 (2H).

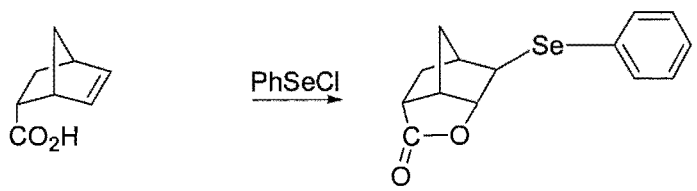
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.90(C1), 67.63(C2), 52.40(C3), 46.99(C4), 42.65(C5), 26.43(C6), 36.14(C7), 129.11(C8), 134.62(C9, C13), 129.40(C9, C12), 127.64(C11).

5-*endo*-phenylselanylamino-2-norbornene (6.19b)

^{1}H NMR (500 MHz, $CDCl_3$),δ 4.42 (1H), 6.45 (1H), 6.17 (1H), 3.02 (1H), 2.49 (1H), 2.36 (1H), 4.94 (1H), 1.43 (1H), 1.22 (1H), 7.54 (3H), 7.67(2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 42.17(C1) 130.90(C2), 134.90(C3), 45.79(C4), 60.34(C5), 35.74(C6), 34.31(C7), 129.40, 134.45,127.86,127.56.

6.4(v) Reactions of 5-*endo*-carboxy-2-norbornene.



(70)

5-*endo*-Carboxy-2-norbornene-6-*endo*-carboxylic acid (50 mg, 0.36 mmol) was dissolved in 1 mL of dichloromethane in a 5 mL vial. To this 80 mg (0.41 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added drop by drop until a slight excess (as indicated by the reaction mixture

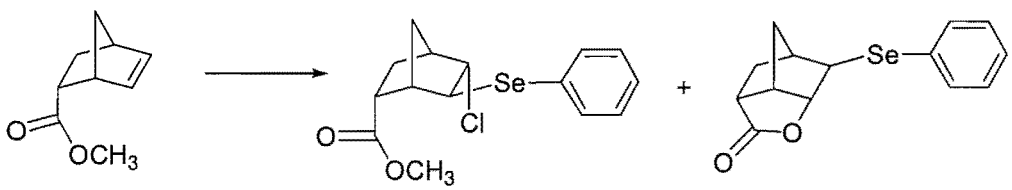
acquiring an orange colour) was present. The solution was then stirred at room temperature for 10 minutes. The reaction appeared quite fast. The solvent was then removed by evaporation under reduced pressure at room temperature. ^{1}H NMR analysis of the product showed the presence of a single product, the lactone (**70**). The identity of this compound was confirmed by X-ray crystallography[102] This compound was subsequently found to have been previously prepared by Nicolaou and coworkers[99-101,167] by this reaction.

5-*endo*-hydroxy-3-*endo*-carboxy-2-*exo*-phenyselanyl[2.2.1]bicycloheptane lactone(70)

^{1}H NMR (500 MHz, $CDCl_3$), δ 3.23 (dd, 1H J = 1.0, 4.9 Hz, H1), 4.73 (d, 1H J = 4.9 Hz, H2x), 3.32 (bd, 1H J = 2.0 Hz, H3n), 2.51 (d, 1H J = 2.9 Hz, H4).), 2.09 (m, 1H J = 3.9, 9.3, 11.2 Hz, H5x), 1.78 (t, 1H J = 2.0,11.2 Hz, H5n), 2.56 (dd, 1H J = 4.4, 11.2 Hz, H6x), 1.66 (dd, 1H J = 1.5 Hz, H7s), 2.20 (dd, 1H J = 1.5 Hz, H7a), 7.27 (1H), 7.28 (2H), 7.50 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 46.29(C1), 86.26(C2), 49.15(C3), 42.12(C4), 35.09(C5), 38.14(C6), 36.60(C7), 179.98(CO), 128.53(C8), 132.84 (C9, C13), 129.25(C10, C12), 127.39(C11).

6.4(vi) Reaction of 5-*endo*-methoxycarbonyl–2-norbornene



6.21 **(70)**

5-*endo*-Carbomethoxy-2-norbornene (20 mg, 0.13 mmol) was dissolved in 1 mL of dichloromethane. To this solution 25 mg (0.13 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added dropwise and the solution stirred at room temperature for 10 minutes. The solvent was then removed under reduced pressure on a cold water bath. The product composition was examined by ^{1}H NMR. The ratio of the two addition products present ((**6.21**) and (**70**) was 80:20. The mixture was purified by passage through a dry silica

column (1:30, the ratio of compound to silca gel by weight), eluting with 80:20 petroleum ether:ethyl acetate. The first fraction that came off was (**6.21**). The second fraction collected was (**70**).The structure of this was confirmed by determining its structure by single crystal x-ray crystal diffraction and the crystal structure published in Acta Crystallogr. Section E.

2-*endo*-chloro-5-*endo*-methoxycarbonyl-3-*exo*-phenyselanyl[2.2.1] bicycloheptane (6.21)

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.48 (dt, 1H J = 1.5, 2.4, 7.3, 9.8 Hz, H1), 4.11 (t, 1H J = 2.0, 6.3 Hz, H2n), 3.22 (dd, 1H J = 2.9, 4.4, 7.3 Hz, H3n), 2.67 (s, 1H, H4), 2.91 (td, 1H J = 2.0, 4.4, 5.4,6, 3 Hz, H5x), 2.45 (dd, 1H J = 2.4, 2.9, 5.4, 8.3 Hz, H6x), 1.72 (d, 1H J = 4.9 Hz, H6n), 1.61 (t, 1H J = 1.5, 3.4 Hz, H7s), 1.93 (t, 1H J = 9.3, 10.7 Hz, H7a), 3.57 (OCH_3),7.26-7.30 (3H), 7.54-7.57 (2H).

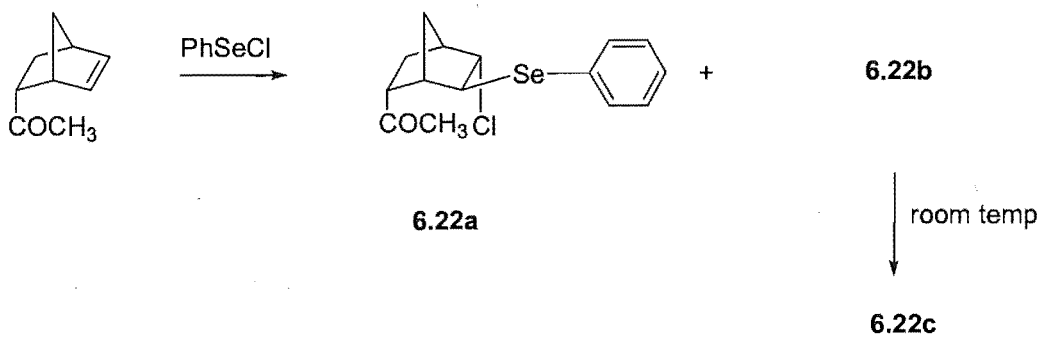
^{13}C NMR (75 MHz, $CDCl_3$), δ 44.88(C1), 66.34(C2), 48.86(C3), 47.58(C4), 46.06(C5), 23.68(C6), 37.21(C7), 173.19(CO), 51.53(OCH_3), 129.05(C8), 133.57(C9,C13), 129.54(C10,C12), 127.45(C11).

3-*endo*-hydroxy-5-carboxy-2-*exo*-phenylselanyl[2.2.1]bicycloheptane lactone(70)

^{1}H NMR (500 MHz, $CDCl_3$), δ 3.23 (dd, 1H J = 1.0, 4.9 Hz, H1), 4.73 (d, 1H J = 4.9 Hz, H2x), 3.32 (bd, 1H J = 2.0 Hz, H3n), 2.51 (d, 1H J = 2.9 Hz, H4).), 2.09 (m, 1H J = 3.9, 9.3, 11.2 Hz, H5x), 1.78 (t, 1H J = 2.0, 11.2 Hz, H5n), 2.56 (dd, 1H J = 4.4, 11.2 Hz, H6x), 1.66 (dd, 1H J = 1.5 Hz, H7s), 2.20 (dd, 1H J = 1.5 Hz, H7a), 7.27 (1H), 7.28 (2H), 7.50 (2H).

^{13}C NMR (75 MHz, $CDCl_3$),δ 46.29(C1), 86.26(C2), 49.15(C3), 42.12(C4), 35.09(C5), 38.14(C6), 36.60(C7), 179.98(CO), 128.53(C8), 132.84 (C9, C13), 129.25(C10, C12), 127.39(C11).

6.4(vii) Reaction of 5-*endo*-acetyl-2-norbornene



5-*endo*-Acetyl-2-norbornene (35 mg, 0.26 mmol) was dissolved in 1 mL of dichloromethane in a 5 mL vial. To this solution 50 mg, (0.26 mmol) of phenylselenyl chloride dissolved in 1 mL of dichloromethane was added dropwise and the solution was stirred at room temperature for 15 minutes. The solvent was then removed under reduced pressure. ^{1}H NMR analysis of the product showed the presence of (**6.22a**). There was also apparently another product formed (**6.22b**), but this appeared to decompose rapidly at room temperature. to give (**6.22c**).The ^{1}H NMR spectrum of the mixture was not good enough for the latter compound to be identified.

5-*endo*-acetyl-2-*endo*-chloro-3-*exo*-phenyselanyl[2.2.1]bicycloheptane (6.22a)

^{1}H NMR (500 MHz, $CDCl_3$) ,δ 2.24 (1H, H1), 4.36 (1H, H2), 2.88 (1H, H3), 3.24 (1H, H4), 2.10(CH_3), 2.01 (1H, H5x), 1.72 (1H, H6x), 1.49 (1H, H6n), 1.34 (1H), 1.20 (1H).(not resolved to get the proper couplings).

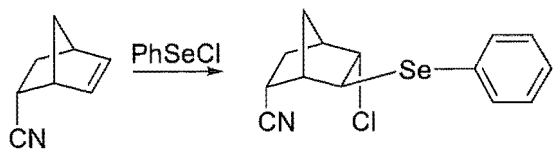
^{13}C NMR (75 MHz, $CDCl_3$),δ 44.19(C1), 65.94(C2), 53.96(C3), 46.76(C4), 54.12(C5), 34.25(C6), 47.45(C7), 25.04(CH_3), 208.84(CO), 129.24(C8), 134.23(C9, C13), 129.26(C10, C12) , 127.69(C11).

Unknown compound (6.22c)

^{1}H NMR, $CDCl_3$), δ 4.79 (1H), 3.53 (1H), 3.19 (1H), 3.12 (1H), 2.35 (1H), 2.20 (1H), 2.11 (1H), 1.60 (1H), 1.40 (1H), 1.21 (1H), 0.91 (1H).(the couplings could not be resolved).

^{13}C NMR, $CDCl_3$),δ 80.44, 50.29, 46.30, 45.51, 41.56, 32.81, 210.53, 132.66, 129.96, 126.84, 125.51.

6.4(viii) Reaction of 5-*endo*-cyano-2-norbornene



6.23

5-*endo*-Cyano-2-norbornene (50 mg, 0.42 mmol) was dissolved in 1.5 mL of dichloromethane. To this phenylselenyl chloride (50 mg, 0.26 mmol) dissolved in 1.5 ml of dichloromethane was added dropwise, and the reaction stirred at room temperature. The addition reaction was slow (based on the rate of decolourisation of the solution) and took 40 minutes to complete. The solvent was removed under reduced pressure and the residue analysed. Analysis of the crude product by ^1H NMR showed only one addition product (**6.23**). (Some unreacted 5-*endo*-cyano-2-norbornene was also present.) When the experiment was repeated using excess PhSeCl under same conditions, two addition products were obtained in a ratio of 88.4:11.6. The first was (**6.23**) and the second its phenydichloroselanyl analogue. Chromatography using a dry silica column (1:20) and eluting with 70:30, petroleum ether:ether gave phenyselenenyl chloride as the first fraction and (**6.23**) as the second. The structure was further confirmed by X-ray analysis.

2-*endo*-chloro-5-*endo*-cyano-3-*exo*-phenylselanyl[2.2.1]bicycloheptane (6.23)

^1H NMR (500 MHz, $CDCl_3$), δ 2.56 (s, 1H, H1), 4.18 (dd, 1H J = 1.5, 5.9 Hz, H2x), 3.67 (t, 1H J = 2.9, 7.3 Hz, H3n), 2.57 (d, 1H J = 1.5 Hz, H4), 2.88 (dt, 1H J = 2.9, 4.4, 4.9, 9.3 Hz, H5x), 2.33 (m, 1H J = 2.4, 5.4, 7.8 Hz, H6x), 1.94 (m, 1H J = 2.4, 3.9, 7.8 Hz, H6n), 1.53 (dt, 1H J = 1.5, 2.9, 8.3 Hz, H7a), 2.00 (t, 1H J = 1.0, 10.3 Hz, H7s), 7.30-7.32 (3H), 7.57-7.59 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 47.03(C1), 65.68(C2), 47.93(C3), 44.50(C4), 30.52(C5), 26.89(C6), 36.44(C7), 127.99(C8), 133.76(C9, C13), 129.40(C10, C12), 128.53(C11).

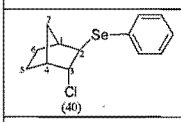
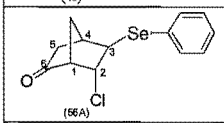
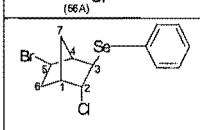
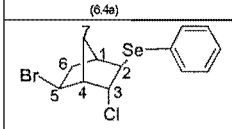
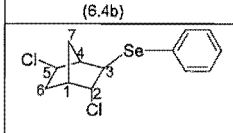
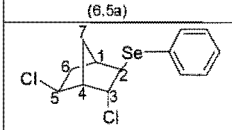
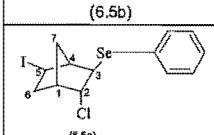
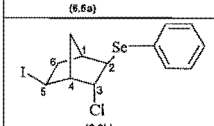
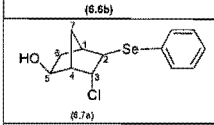
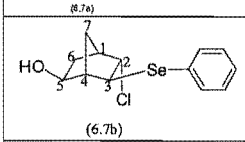
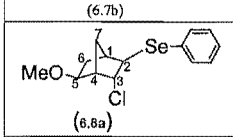
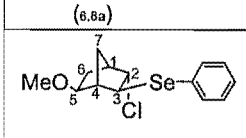
6.5 Assignment of ^{1}H NMR spectra of products.

The structure of new products presented here were based on their 500 MHz ^{1}H and 75 MHz ^{13}C NMR spectral data. Signal assignments in the 500 MHz ^{1}H NMR spectra were based on HSQC, CIGAR and 1DNOESY experiments. The *trans* relationship between the phenylselanyl and chloro substituents was based on the coupling constants of their geminal protons to neighbouring ones. The *exo* and *endo* protons at C5 and C6 in the phenylselenyl chloride adducts to norbornene was established by Carrupt and Vogel[73]on the basis of their vicinal coupling constants with the adjacent bridgehead protons H1 and H4, in some cases with the additional help of H7a or H7s. It has been reported that the *cis*-vicinal coupling constants between pairs of *endo* hydrogens are appreciably different from the *cis*-vicinal constants between pairs of exo ones, even though the substituents and dihedral angles are the same in both cases.[168,169]. The assignment of the position of the *endo* substituent was based on the coupling between the *exo* H2 and the bridgehead proton H1 and the *exo* H3x with the bridgehead H4 proton. Literature values for this coupling vary between 3.2-3.9 Hz.[170] For the *exo* isomer no coupling or connectivity is observed between *endo* H2 proton to H1 or *endo* the 3n proton to H4. There is a strong coupling observed between the *exo* H2x and *exo* H3x protons in *endo* substituted norbornenes. The order of coupling constants are *exo-exo* > *exo-endo* >*endo-endo*[168,171,172]. Once these couplings are located it is very easy to assign the other protons. In the adduct systems one more coupling is necessary to establish the stereo and regio-chemistry of the product. This is the coupling between the C2 or C3 *endo* hydrogen and the C7 *anti* hydrogen, which is nearly 2.9 Hz. The non equivalence is also known for vicinal proton-proton coupling constants $^{3}J_{HH}$. However the norbornenes I investigated contain a substituent at C5 that had an effect on the dihedral angle. As a result the coupling constants are found to vary, which are reflected in the given values (Tables 6.1 and Table 6.2).

Phenylselenyl chloride adds to the double bond of 5-*exo* and 5-*endo* 2-norbornenes stereoselectively giving the products in which the chloride takes up

an *endo* site at C2 (or C3) and the phenylselanyl group the *exo* site at C3 (or C2) respectively. The product ratios were determined by integration of the hydrogens on the carbons to which these are bonded. Whether these C2 and C3 protons are *exo* or *endo* protons is determined from their vicinal couplings as described in previous paragraph. The ^{1}H assignments and regiochemistries of the products were unambiguously assigned from the 500 MHz ^{1}H NMR spectra and were found to be in agreement with the reported literature ones where these were available.[173,174] The data assignments have been given in the experimental section, but for convenience are summarised in Tables 14 and 15.(see following pages)

Table 14. A summary of the experimental values of the ^{1}H chemical shifts of the phenylselenyl chloride adducts of 5-*exo* substituted 2-norbornenes

^{1}H NMR ($CDCl_3$,500 MHz) and ^{13}C NMR ($CDCl_3$,75 MHz) data of phenyselenyl chloride added 5-exosubstituted-2-norbornanes. δ (H) ppm,J(H,H)Hz, x=exo, n=endo,s=syn, a=anti (Protons in same order as in figure).	
	H_1, H_{2n}, H_{2x} H_{3n}, H_{3x},H_4, H_{5n}, H_{5x},H_{6n}, H_{7a}, H_{7s}(given in order)
 (40)	2.35 (bd,4.4), 3.12 (t,3.4),.4.17 (t,2.0,4.4), 2.45(t,4.0,8.9), 1.99 (m) 1.45(m), 1.68 (dt,4.9, 9.3), 1.36 (m), 1.79 (d,10.7), 1.43 (t,3.4,4.9).
 (56A)	2.87 (d,3.4), 4.30 (3.4,7.8), 3.44 (t,2.9,5.9), 2.74 (t,1.5,3.4), 2.31 (dd,4.9,5.4), 2.06 (d,4.4), 2.21 (dt, 1.5,2.9,8.3), 1.88 (t,1.5,11.7).
 (6.4a)	2.52 (m), 4.13 (t,2.0,4.4), 2.97 (t,3.4,7.3), 2.61 (s), 4.00 (dt,2.0,4.4,4.9,7.8), 2.84 (td,2.4,2.9,11.2), 2.04 (m), 1.84 (td,1.5,2.0,3.4), 2.08 (m).
 (6.4b)	2.40 (t,1.5,2.9), 3.04 (t,2.9,6.8), 4.20 (t,3.9,8.3), 2.79 (t,2.4,6.8), 4.64 (m). 2.23 (t,1.5,4.4), 2.22 (t,1.5,5.9), 1.93 (dt,1.5,2.9,8.3,11.2), 2.12 (t,1.5,2.9)
 (6.5a)	2.55 (m), 4.10 (dt,1.5,2.0,4.4), 2.95 (dd,2.9,4.4), 2.70 (bs), 3.93 (td,2.0,3.4,3.9,7.8), 2.72 (m), 1.77 (m), 1.81 (d,2.4), 2.01 (m).
 (6.5b)	2.42 (d,3.9), 3.05 (t,3.4), 4.20 (t,4.4), 2.72 (dd,2.4,7.3), 4.58 (dt,2.4,2.9,4.4,7.3), 2.15 (4d,2.0,2.4,6.8,7.3), 2.03 (dt,1.5,3.4,4.9,8.3), 1.89 (dt,1.5,3.4,3.9,7.3), 2.04 (m).
 (6.6a)	2.68(bs), 4.14 (td,2.4,4.4,5.9), 3.07 (d,4.4), 2.44 (t,1.5,5.4), 3.99 (m), 2.86 (td,2.0,2.4,7.8), 2.15 (dd,1.5,4.9),1.90 (dt,1.5,2.4,3.9,7.3), 2.13 dt,1.5,2.9,4.9,9.8),.
 (6.6b)	2.32 (d,2.0), 3.04 (d,4.4), 4.12 (td,2.0,4.4,5.9), 2.84 (d,2.4), 4.67 (m), 2.35 (t,4.9,8.8), 2.27 (td,2.0,2.9,5.4), 1.99 (m), 2.14 (m), .
 (6.7a)	2.37 (d,4.4), 3.05 (2.9,5.9), 4.14 (t,4.4,8.3), 2.47 (d,3.9), 4.50 (d,6.9), 1.53 (dt,1.5,2.4,3.9,11.2), 1.90 (ddd,2.4,6.9,9.3), 1.65 (m), 1.83 (m).,
 (6.7b)	2.43 (dd,2.4,6.8), 4.08 (dd,3.9,5.9), 3.87 (d,6.8), 2.87 (t,2.9,7.3), 4.33 (t,5.9,6.9), 1.67 (d,6.9,not completely resolved), 2.14 (m), 1.32 (dt,2.4,2.9,8.8,11.2), 1.82 (dd,2.0,2.4).
 (6.8a)	2.34 (d,2.4), 3.06 (dd,2.0,4.4), 4.16 (t,4.4), 2.62 (d,4.4), 3.95 (dd,2.4,6.8), 1.58 (m), 1.81 (m), 1.70-1.72 (7a,7s).
 (6.8b)	2.34 (d,4.9), 4.12 (td,2.0,3.9,5.4), 2.87 (q,2.4,2.9,3.9), 2.45 (d,5.4), 3.35 (d,6.8), 1.34 (dt,2.0,2.4,4.9), 2.36(m), 1.74 (t,1.5,4.0), 1.63 (m).

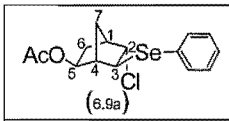
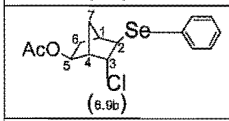
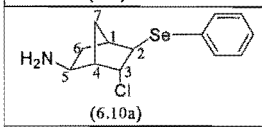
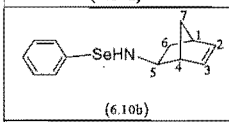
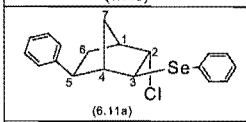
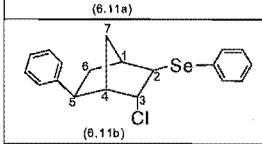
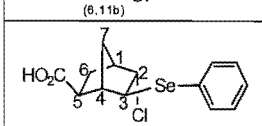
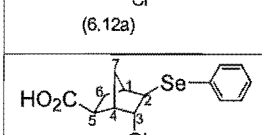
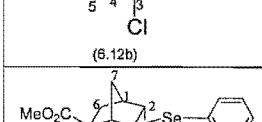
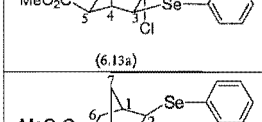
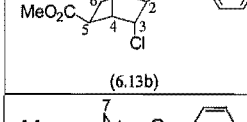
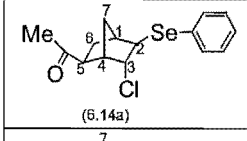
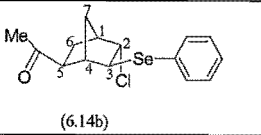
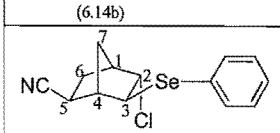
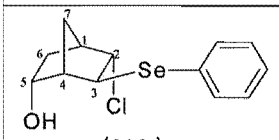
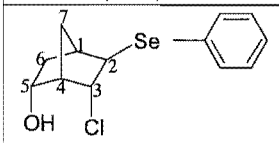
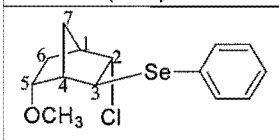
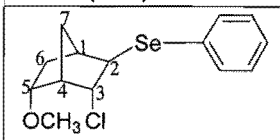
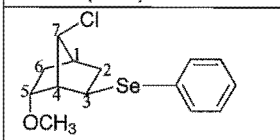
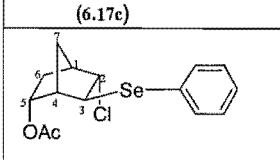
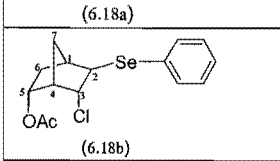
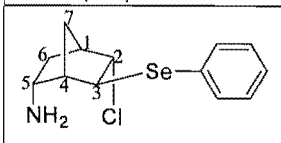
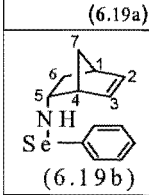
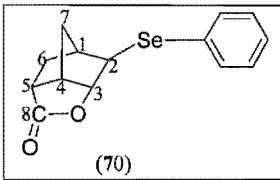
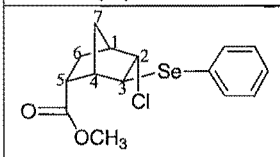
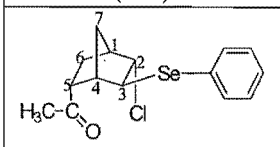
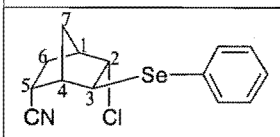
 (6.9a)	2.51 (m), 4.09 (t,2.9,4.4), 2.99 (t,2.9,6.3), 2.43 (s), 4.70 (d,6.3), 1.44 (dt,2.0,2.8,4.4), 2.54 (dd,2.0,7.3), 1.72(m), 1.74 (m).
 (6.9b)	2.39 (d,3.9), 3.09 (t,2.9,5.9), 4.15 (t,3.9,4.4), 2.65 (d,3.9), 5.29 (d,6.3), 1.64 (m), 2.03 (t,2.8,4.8), 1.76 (dd,2.0,4.0), 1 80(m).
 (6.10a)	2.66, 3.14, 4.15, 2.78, 2.97, 1.98, 1.85, 1.72, 1.66. (the proton spectra forms broad peaks).
 (6.10b)	6.20, 6.02, 3.94, 3.29, 3.02, 2.86, 2.58, 2.21, 1.90 (broad spectrum).
 (6.11a)	2.60 (s), 4.21 (d,4.4), 3.32 (t,2.4,5.4), 2.53 (d,1.5), 2.94 (dd,5.4,5.9), 1.69 (dd,3.9,5.4), 2.57 (d,3.4), 1.66 (t,4.4,5.9), 1.74 (s).
 (6.11b)	2.47 (s), 3.20 (d,3.4), 4.25 (1.5,4.9), 2.57 (d,3.4), 3.61 (t,7.3,7.8), 1.91 (d,2.4), 1.92 (d,3.9), 1.71 (t,1.5,5.9), 1.76 (d,1.5).
 (6.12a)	2.53 (d,4.4), 4.16 (t,3.9,7.8), 3.13 (t,2.9,5.4), 2.66 (s), 2.52 (d,5.4), 1.85 (t,4.9), 2.31 (t,10.7,11.7), 1.82 (dd,3.9,8.3), 1.71 (dd,1.5,11.2).
 (6.12b)	2.40 (d,3.9), 3.08 (t,3.4,6.3),, 4.19 (t,4.4), 2.80 (d,3.9), 3.20 (dd,5.4,9.3), 1.73 (t,9.8,12.2), 2.04 (dt,4.4,9.8,12.7), 1.83 (d,2.00, 1.64 (1.5,11.2).
 (6.13a)	2.54 (bd), 4.17 (dd,3.9,5.9), 3.13 (dd,4.0,5.2), 2.64 (s), 2.51 (dd,5.2,9.1), 1.84 (m), 2.29 (dt,2.0,2.4,3.9,6.3), 1.78 (m), 1.71 (t,1.6,2.8).
 (6.13b)	3.17 (dd,5.2,9.2), 3.08 (t,1.2,4.0), 4.19 (t,2.0,6.7), 2.76 (dd,2.8,6.7),), 2.40 (bd,3.6), 1.64 (td,1.6,2.7,8.3), 2.05 (dt,5.2,9.21.80 (m), 1.69 (m).
 (6.14a)	2.50 (s), 3.17 (t3.4,6.3), 4.18 (dt,2.0,3.9,5.9,8.3), 2.56 (s), 2.56 (dd,3.4,6.3), 1.81 (m), 2.17 (m), 1.49 (dt,1.5,4.4,6.3,7.8), 1.72 (m).
 (6.14b)	2.69 (dd,1.5,3.9), 4.21 (t,4.4,8.3), 3.09 (dd,2.9,3.9), 2.39 (3.4), 3.23 (dd,5.3,8.3), 1.54 (dd,2.9,12.2), 2.04 (dt,2.9,4.9,9.3,12.2), 1.44 (1.5,2.0,4.9,6.3), 1.70 (dd,1.5,3.9).
 (6.15a)	2.63 (s), 4.11 (td,1.5,2.0,6.8,9.8), 2.98 (t,2.9,6.8), 2.58 (d,3.9), 2.47 (t,1.0,1.5), 2.48 (t,1.5,2.4), 1.77 (td,1.5,3.9,5.9,12.7), 1.93 (s), 1.80(m).
 (6.15b)	2.45 (t,2.0,2.4), 3.03 (t,3.4), 4.17 (t,3.9,4.4), 2.79 (d,3.9), 3.23 (dd,4.4,4.9), 1.86 (m), 1.99 (m), 1.96 (d,4.4), 1.83 (t,1.0,2.9).

Table 15 A summary of the experimental values of the ^{1}H chemical shifts of 5-*endo* substituted norbornenes after the addition of phenylselenyl chloride.)

^{1}H NMR ($CDCl_3$,500 MHz) and ^{13}C NMR ($CDCl_3$,75 MHz) data of phenyselenyl chloride added 5-endosubstituted-2-norbornanes. δ (H) ppm, J(H,H)Hz, x=exo, n=endo,s=syn, a=anti	
	H_1 H_{2n} H_{2x} H_{3n} H_{3x} H_4 H_5 H_{5x} H_{6n} H_{7a} H_{7s} (given in order)
 (6.16a)	2.40 (d,3.9), 4.27 (dd,2.9,4.4), 3.90 (dd,2.9,4.4), 2.39 (s), 4.31 (t,3.9,5.4), 1.73 (t,3.4), 1.89 (td,2.9,3.9,4.9), 1.78 (d,11.2),1.52 (d,11.2).
 (6.16b)	2.34 (s), 3.45 (t,3.4,7.3), 4.34 (t,3.9,5.4), 2.64 (bs), 4.36 (t,3.9,5.4), 1.45 (bd,11.2), 1.73 (t,3.4,7.3), 2.37 (s), 1.24 (t,4.4,12.2).
 (6.17a)	2.40 (bs), 4.21 (t,3.4,7.8), 3.70 (dd,2.9,4.9), 2.53 (t,2.4,3.9), 3.77(m), 1.43 (dd,3.4,7.8), 1.79 (t,3.4,7.8), 1.81 (dd,1.5,4.4), 1.50 (t,1.0,2.4).
 (6.17b)	2.45 (s), 2.72 (bd), 4.37 (dd,1.5,3.9), 3.39 (s), 3.83 (d,3.9), 1.22 (t,3.9,7.5), 2.17 (m), 1.61 (t,3.4,7.3), 1.85 (t,1.2,3.6).
 (6.17c)	3.60 (t,3.9), 2.91 (m), 1.53 (t,1.5,2.9), 0.96 (t,2.0,3.4), 2.46 (d,6.3), 3.85 (d,2.8), 1.41 (d,2.0), 1.91 (dd,2.0,3.4), 4.30 (t,2.4,4.9).
 (6.18a)	2.45 (d,3.9), 4.23 (dt,1.5,4.4,5.9), 3.68 (t,2.9,4.9), 2.60, (t,3.4,4.4), 5.03 (dt,2.0,3.9,8.3,10.3), 1.86 (dt,3.5,3.9,6.3,7.3), 1.98 (m), 1.80 (t,1.5,3.4), 1.58 (dd,1.5,8.3).
 (6.18b)	2.59 (bs), 3.01 (t,2.9,4.4), 4.17 (t,4.4,7.3), 2.87 (dd,2.9,4.9), 5.21 (dd,2.9,5.4), 1.75 (dd,3.9,10.7), 2.28 (dd,4.4,4.9), 1.33 (dd,1.5,11.2), 1.02 (t,3.4).
 (6.19a)	4.26, 4.04, 3.76, 2.76, 2.43, 2.02, 1.99, 1.79, 1.57 (broad spectrum)
 (6.19b)	6.45, 6.17, 4.94, 4.42, 3.02, 2.49, 2.36, 1.43, 1.22. (broad spectrum).

 (70)	2.51 (d,2.9), 4.73 (d,4.9), 3.32 (bd,2.4), 3.23 (dd,1.0,4.9), 2.56 (dd,4.4,11.2),2.09 (m), 1.78 (t,2.0,11.7), 2.20 (dd,1.5), 1.66 (dd,1.5.11.2).
 (6.21a)	2.48 (dt,1.5,2.4,7.3,9.8), 4.11 (t,2.0,6.3), 3.22 (dd,2.9,4.4), 2.67 (s), 2.91 (td,2.0,4.4,5.4,6.3), 1.72 (d,4.90), 2.45 (td,2.4,2.9,5.4), 1.93 (t,9.3,10.7), 1.61 (t,1.5,3.4).
 (6.22a)	4.36 (1H), 3.24 (1H), 2.88 (1H), 2.24 (1H), 2.10(CH3), 2.01 (1H), 1.72 (1H), 1.49 (1H), 1.34 (1H), 1.20 (1H).(not resolved to get the proper couplings).
Unknown	4.79 (1H), 3.53 (1H), 3.19 (1H), 3.12 (1H), 2.35 (1H), 2.20 (1H), 2.11 (1H), 1.60 (1H), 1.40 (1H), 1.21 (1H), 0.91 (1H).
 (6.23)	2.56 (s), 4.18 (dd,1.5,5.9), 3.67 (t,2.9,7.3), 2.57 (d,1.5), 2.88 (dt,2.9,4.4,4.9,9.3), 1.94 (m), 2.33 (m), 1.53 (dt,1.5,2.9,8.3,11.2), 2.00 (t,1.0,10.3).

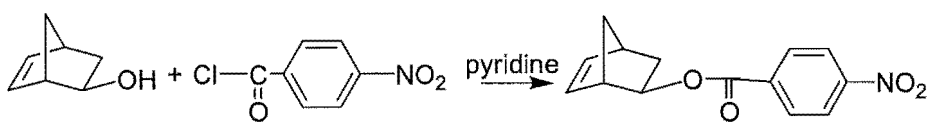
Chapter 7.

EXPERIMENTAL PART 3: Preparation of solid esters of 5-hydroxy-2-norbornene for X-ray study

General procedure

These esters were prepared using literature procedures, but slight changes were sometimes necessary. In all but one case the appropriate *exo* or *endo* 5-hydroxy-2-norbornene was dissolved in a mixture of dry methylene chloride and pyridine containing a catalytic amount of 4-dimethylaminopyridine and a freshly prepared sample of the appropriate aroyl chloride was then added. After stirring at room temperature for 12 to 48 hours the mixture was quenched with water and extracted with dichloromethane. The pyridine was removed by washing with $CuSO_4$ solution, and the crude product purified by column chromatography on dry silica using ethyl acetate-petroleum ether as eluant. The yield obtained was typically 80-95%.

7.1 ***exo*-Bicyclo[2.2.1]hept-5-en-2-yl 4-nitrobenzoate**[81,175-177]



7.1

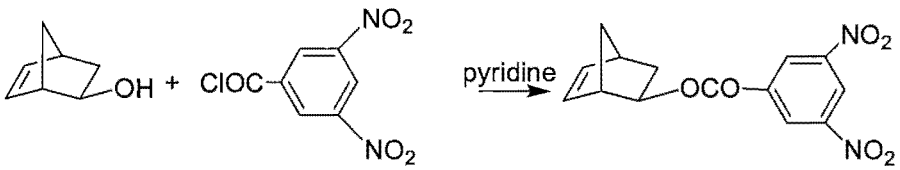
5-*exo*-Hydroxy-2-norbornene (150 mg, 1.35 mmol) was dissolved in 3 mL of anhydrous CH_2Cl_2 in 100 mL R.B flask and to this two crystals of DMAP were added. To this solution 0.8 mL of anhydrous pyridine was added and the mixture stirred. To this stirred solution1 g, (5.4 mmol) of freshly prepared[175] 4-nitro benzoyl chloride was added. The flask was fitted with a $CaCl_2$ drying tube and the mixture was stirred for 16 hours at room temperature. The mixture was then quenched by adding 4 mL of water. The benzoate ester formed was then extracted

four times with 15 mL of CH_2Cl_2. The dichloromethane extract was washed with 10 mL of saturated copper sulphate solution, 10 mL of water and finally with 10 mL of brine solution. The CH_2Cl_2 layer was dried over anhydrous $MgSO_4$.and solvent removed by vacuum evaporation. The residue was further purified by silica column chromatography (1:20) using eluent petroleum ether:ethyl acetate, 80:20 ratio. The first fraction collected was the pure *exo* benzoate ester (**7.1**). The crystal for X-ray study was grown by the slow evaporation of a solution of the ester in anhydrous dichloromethane at room temperature. Its melting point was 84.5 °C. The yield was 330 mg (93%).

^{1}H NMR (500 MHz , $CDCl_3$), δ 2.94 (s, 1H, H1), 6.32 (dd, 1H J = 2.9, 5.9 Hz, H2), 6.04 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.05(s, 1H, H4), 4.95 (d, 1H J = 6.8 Hz, H5),1.85 (m, 1H J = 2.4, 6.8, 9.3, 12.7 Hz, H6x), 1.68 (t, 1H J = 8.3, 9.3 Hz, H6n), 1.77 (d, 1H J = 8.8 Hz, H7s), 1.59 (dt, 1H J = 2.4, 2.9, 5.4, 12.7 Hz, H7a), 8.28 (2H), 8.20 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 40.64(C1), 141.46(C2), 132.32(C3), 47.37(C4), 76.98(C5), 46.38(C6), 34.76(C7), 164.67(C8), 136.04(C9), 130.57(C9, C14), 123.47(C10, C13), 150.45(C11).

7.2 ***exo*-Bicyclo[2.2.1]hept-5-en-2-yl 3,5-dinitro benzoate**[81,144,160]



7.2

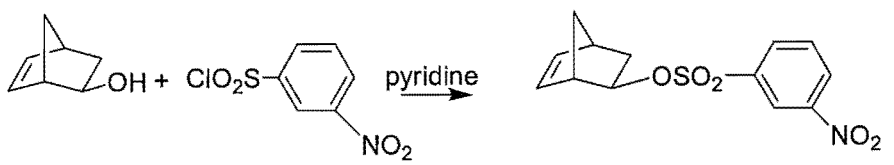
The 5-*exo*-hydroxy-2-norbornene (130 mg, 1.2 mmol) was dissolved in 2.5 mL of anhydrous CH_2Cl_2 in a 100 mL R.B flask and to this two crystals of DMAP and 0.25 mL of anhydrous pyridine were added. To this solution 600 mg (2.7 mmol) of freshly prepared 3,5-dinitrobenzoyl chloride[160] was added and the flask closed with a $CaCl_2$ drying tube. The solution was stirred for 50 hours at room temperature and then quenched by adding 2.5 mL of water. The dinitro ester formed was then extracted three times with 15 mL of dichloromethane. The dichloromethane layer was then washed with 10 mL saturated $CuSO_4$ solution, 10

mL of water and finally with 10 mL of brine solution. The solvent was then removed by rotary vacuum evaporation and the crude residue was further purified by silica column chromatography (1:20). The eluent used was petroleum ether: ethyl acetate, 80:20. The first fraction was pure dinitro ester (**7.2**). Yield = 370 mg, (92.5%), m.p.124.5 °C. A crystal for x-ray study was grown by evaporation of a solution in absolute ethanol at room temperature.

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.98 (s,1H, H1), 6.34 (dd, 1H J = 2.9, 5.4 Hz, H2), 6.05 (dd, 1H J = 2.9, 5.9 Hz,H3), 3.09 (s, 1H, H4), 5.01 (d, 1H J = 6.8 Hz, H5n), 1.89 (m, 1H J = 2.4, 2.9, 6.8, 9.3, 12.7 Hz, H6x), 1.72 (dt, 1H J = 1.5, 2.4, 6.3, 8.8 Hz, H6n), 1.79 (d, 1H J = 8.8 Hz, H7s), 1.64 (dt, 1H J = 2.4, 3.4, 5.9 Hz, H7a), 9.20 (1H), 9.12 (2H).

^{13}CNMR (75 MHz, $CDCl_3$) δ 40.62(C1), 141.65(C2), 132.12(C3), 47.35(C4), 78.25(C5), 46.41(C6), 34.72(C7), 162.45(C8), 134.32(C9), 129.27(C10, C14), 148.56(C11, C13), 122.20(C12).

7.3 *exo*-Bicyclo[2.2.1]hept-5-en-2-yl 3-nitrobenzenesulfonate



7.3

3-nitrobenzenesulfonyl chloride[178]

3-Nitrobenzenesulfonyl chloride had to be freshly prepared for use. Sodium 3-nitrobenzenesulfonate (11 gm, 0.1mol) was heated on a water bath with phosphorus pentachloride (10.5 gm, 0.1mol) in a 250 mL R.B. flask fitted with a $CaCl_2$ drying tube until the mixture melted. The liquid was then heated for a further 8 hours. The $POCl_3$ formed was then distilled off by heating the solution to 110°C. The acid chloride was separated from residual NaCl by extracted the mixture with anhydrous carbon tetrachloride, and the solvent removed by vacuum rotary evaporation. Yield = 11 gm, 87.3%],

exo-bicyclo[2.2.1]hept-5-en-2-yl 3-nitrobenzenesulfonate[178,179]

5-*exo*-Hydroxy-2-norbornene (110 mg, 1 mmol) was mixed with 0.8 mL (9.9 mmol) of pyridine, two crystals of DMAP, and 3 mL of anhydrous dichloromethane in a 100 mL R.B. flask.fitted with a $CaCl_2$ drying tube. To this was added 600 mg (2.7 mmol), of the 3-nitrobenzenesulfonyl chloride. The flask was then stoppered, and the solution stirred for 48hours at room temperature. It was then quenched by adding 5 mL of water. A small amount of dichloromethane was added and organic layer separated. The dichloromethane layer was then washed with 10 mL of 2M hydrochloric acid, followed by 10 mL of water and 10 mL of sodium bicarbonate solution. It was then dried over anhydrous $MgSO_4$, filtered and vacuum evaporated. The crude product was chromatographed using a silica column (1:20) using dichloromethane/petroleum ether as eluent and gave 330 mg of product. This was further purified by dry silica column chromatography (1:20) using 90:10 dichloromethane :petroleum ether. The first fraction to come off was the pure sulphonate ester[180] (**7.3**). The yield was 260 mg (88%), m.p. 79 °C. The crystal for x-ray structure was grown from a 1:1solution of dichloromethane/ethyl acetate.

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.84 (s,1H, H1), 6.23 (dd, 1H J =2.0, 2.4 Hz, H2), 5.92 (t, 1H, J = 2.4, 5.4 Hz, H3), 3.02 (s, 1H, H4), 4.40 (s, 1H, H5n), 1.74 (d, 1H, J = 8.3 Hz, H6x), 1.70 (m, 1H, H6n), 1.60 (m, 1H,H7s), 1.25 (t, 1H J = 3.0, 7.5 Hz, H7a), 8.89 (1H), 8.61 (1H), 8.38 (1H), 7.90 (1H).

^{13}CNMR (75 MHz, $CDCl_3$) δ 40.56(C1), 141.59(C2), 132.22(C3), 48.58(C4), 78.58(C5), 45.93(C6), 35.60(C7), 132.75(C8), 122.43(C9), 145.52(C10), 125.52(C11), 129.52(C12), 131.32(C13),

7.4 ***exo*-Bicyclo[2.2.1]hept-5-en-2-yl 4-bromobenzenesulfonate**[182,183]

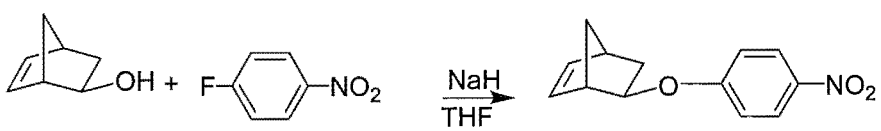
7.4

5-*exo*-Hydroxy-2-norbornene (110 mg, 1 mmol) was dissolved in 2 mL of anhydrous dichloromethane containing 0.5 mL of anhydrous pyridine in 100 mL R.B flask. To this was added 490 mg (1.9 mmol) of 4-bromobenzenesulfonyl chloride.[181] The flask was fitted with a $CaCl_2$ drying tube and the mixture was then stirred for 18 hours at room temperature. The reaction was quenched by adding 3 mL of water and the CH_2Cl_2 layer was separated and washed with 10 mL of saturated $NaHCO_3$ solution, followed by 10 mL saturated $CuSO_4$ solution and finally with 10 mL of water. The CH_2Cl_2 layer was then filtered through a sintered funnel containing anhydrous $MgSO_4$. The solvent was then removed by vacuum rotary evaporation. This residue was extracted with petroleum ether. Evaporation of the solvent gave 302 mg of (**7.4**). 92%. This material was then crystallized from anhydrous petroleum ether. The melting point of the product was 96 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.83 (s,1H, H1), 6.23 (dd, 1H J = 2.9, 5.4 Hz, H2), 5.86 (dd, 1H J = 2.9, 5.9 Hz, H3), 2.95 (d, 1H J = 1.5 Hz, H4), 4.51 (t, 1H J = 2.9, 8.8 Hz, H5n), 1.68 (d, 1H J = 8.3 Hz, H6x), 1.63 (d, 1H J = 2.9 Hz, H6n), 1.60 (m, 1H J = 1.5, 2.4, 3.4, 8.3 Hz, H7s), 1.52 (dt, 1H J = 2.9, 3.4, 5.4, 5.9 Hz, H7a), 7.77 (2H), 7.69 (2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 40.50(C1), 142.22(C2), 131.53(C3), 48.02(C4), 83.61(C5), 46.09(C6), 34.63(C7), 136.40(C8), 132.50(C9, C13), 129.15(C10, C12), 128.67(C11).

7.5 *exo*-Bicyclo[2.2.1]hept-5-en-2-yl 4-nitrophenyl ether



7.5

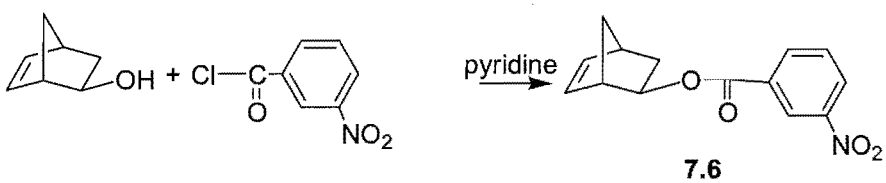
5-*exo*-Hydroxy-2-norbornene (110 mg, 1 mmol) was dissolved in 4 mL of anhydrous THF in a 100 mL R.B. flask and to this 150 mg (6.5 mmol) of NaH washed with pentane and dried by nitrogen was added. The mixture was refluxed on a water bath at 50 °C for 3 hours. The reaction mixture was then cooled to

room temperature and 1.4 gm (0.01 mol) of 4-fluoro-1-nitrobenzene was added and stirred for 24 Hours at room temperature[81,184,185]. It was then quenched with 10 mL saturated NH_4Cl solution and was extracted with DCM. The DCM layer was washed with 10 mL saturated sodium chloride solution and dried over anhydrous Na_2SO_4, filtered and vacuum rotary evaporated. The crude product was further purified by silica column chromatography (1:20), using 90:10, petroleum ether : ethyl acetate eluent. The fraction came first was pure exo-ether (**7.5**). Yield = 200 mg (86%), m.p. 58 °C. This was then crystallized from.by the slow evaporation of a solution of dichloromethane ,ethyl acetate,(70:30).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94 (s, 1H, H1), 6.33 (dd, 1H J = 2.93, 5.9 Hz, H2), 6.04 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.06 (s 1H, H4), 4.34 (d, 1H J = 6.3 Hz, H5n), 1.52 (dt, 1H J = 2.9, 5.9, 6.8, 12.7 Hz, H6n), 1.83 (t, 1H J = 2.9, 6.3 Hz, H6x), 1.80 (t, 1H J = 3.4, 9.3 Hz, H7s),1.67 (d, 1H J = 8.3 Hz, H7a), 8.18 (2H), 6.92 (2H).

^{13}C NMR (75 MHz, $CDCl_3$), δ 40.77(C1), 141.74(C2), 132.20(C3), 47.23(C4), 79.06(C5), 46.36(C6), 35.05(C7), 163.58(C8), 125.85(C9, C13), 115.13(C10, C12) 141.14(C11).

7.6 *exo*-Bicyclo[2.2.1]hept-5-en-2-yl 3-nitrobenzoate



7.6

3-nitrobenzoyl chloride[178]

This was prepared by heating a mixture of 3 gm of 3-nitrobenzoic acid and 3 gm of PCl_5 together for about two minutes. The $POCl_3$ by product was removed by evaporation and the residue was then poured into watch glass and allowed to solidify.

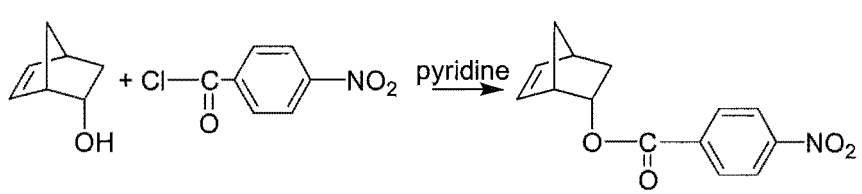
Exo-bicyclo[2.2.1]hept-5-en-2-yl 3-nitrobenzoate[81]

The 5-*exo*-hydroxy-2-norbornene (110 mg, 1 mmol) was dissolved in 3 mL of anhydrous CH_2Cl_2. To this 0.3 mL of anhydrous pyridine and two crystals of DMAP were added and the solution stirred for a short time. The freshly prepared 3-nitrobenzoyl chloride (600 mg, 3.2 mmol) was added, the flask closed with a stopper and the solution stirred for 24hours at room temperature[175,176,186]. The reaction mixture was then quenched with 3 mL of water and the ester was extracted with dichloromethane. The dichloromethane layer was then washed with 10 mL of saturated $CuSO_4$ solution, 10 mL of water and finally with 10 mL of saturated brine solution. The organic layer was vacuum rotary evaporated. The crude product further purified by dry silica column chromatography (1:40), using 80:20 petroleum ether:ethyl acetate as eluent. The undissolved brown residue was discarded. The fraction coming off the column was was the pure ester (**6.6**). Yield = 240 mg (94.5%), m.p. 50 °C. This was then crystallized from anhydrous dichloromethane.

^{1}H NMR ($CDCl_3$ 500 MHz), δ 2.94 (s,1H, H1), 6.32 (dd, 1H J = 2.9, 5.9 Hz, H2), 6.04 (dd, 1H J = 3.4, 5.4 Hz,H3), 3 06 (s, 1H, H4), 4.96 (d, 1H J = 7.3 Hz, H5n), 1.85 (m, 1H J = 2.4, 2.9, 7.3, 9.8, 12.7 Hz, H6x), 1.60 (dt, 1H J = 2.9, 5.9, 6.8, 12.7 Hz, H6n), 1.78 (d, 1H J = 8.8 Hz, H7s), 1.68 (d,1H J = 8.3 Hz, H7a), 8.82 (t, 1H J = 1.5, 3.4 Hz), 8.40 (dd, 1H J = 1.5, 7.8, 8.8 Hz), 8.38 (dd, 1H J = 0.98, 7.8 Hz), 7.65 (t, 1H J = 7.8, 8.3 Hz).

^{13}C NMR (75 MHz, CDC_3) δ 40.65(C1), 141.47(C2), 132.45(C3), 47.39(C4), 77.00(C5), 46.43(C6), 34.75(C7), 164.45(C8), 132.36(C9), 148.23(C10), 124.42(C11), 127.25(C12), 129.56(C13), 135.22(C14). (The C5 carbon of the norbornene ring overlaps with 77.00 ppm carbon of the $CDCl_3$ (This could be shown by changing the NMR solvent to DMSO.)

7.7 *endo*-Bicyclo[2.2.1]hept-5-en-2-yl 4-nitrobenzoate



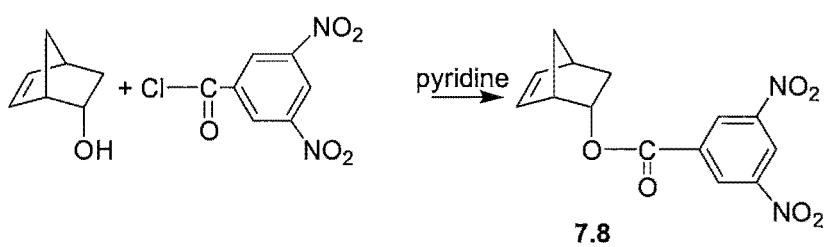
7.7

5-*endo*-hydroxy–2-norbornene (110 mg, 1 mmol) was dissolved in 2.5 mL of anhydrous CH_2Cl_2 in a 100 mL R.B flask and two crystals of DMAP was added to this. The solution was then stirred with 0.3 mL of anhydrous pyridine[186]. To this mixture 420 mg, (2.4 mmol)of freshly prepared *p*-nitrobenzoyl chloride[175]was added, the flask capped with a $CaCl_2$ drying tube and the solution was stirred for 14hours at room temperature. The reaction mixture was then quenched with water (2 mL) and the benzoate ester product was then extracted with three 15 mL portions of dichloromethane. The dichloromethane layer was washed successively with 10 mL of saturated $CuSO_4$ solution, 10 mL of water and 10 mL of saturated brine solution. The organic layer was then vacuum evaporated without drying and the crude residue was subjected to silica column chromatography (1:20) using 20:80 ethyl acetate:petroleum ether as eluent. The first fraction consisted of impurities but the second fraction was pure ester (**6.7**). Yield = 230 mg (89%), m.p. 83 °C. This was then crystallized from anhydrous dichloromethane.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.93 (d, 1H J = 1.5 Hz, H1), 6.41(dd, 1H J = 2.9, 5.4 Hz, H2), 6.06 (dd, 1H J = 2.9, 5.9 Hz, H3), 3.28 (s, 1H, H4), 5.56 (dt, 1H J = 2.9, 6.8, 11.7 Hz, H5x), 1.55 (m, 1H J = 1.9, 3.9, 5.9, 7.3, 9.3 Hz, H6n), 2.28 (m, 1H J = 1.9, 3.9, 4.4, 5.9 Hz, H6x), 1.42 (d, 1H J = 1.5 Hz, H7s), 1.10 (dt, 1H J = 2.9, 3.4, 6.3 Hz, H7a).8.25 (2H), 811 (2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 42.27(C1), 138.92(C2), 131.24(C3), 47.71(C4), 76.73(C5), 45.90(C6), 34.78(C7), 164.70(C8), 135.86(C9), 130.53(C10, C14), 123.40(C11, C13), 150.36(C12).

7.8 *endo*-Bicyclo[2.2.1]hept-5-en-2-yl 3,5-dinitro benzoate



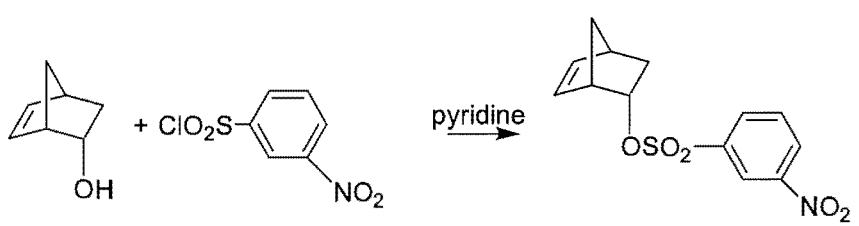
7.8

The 5-*endo* hydroxy-2-norbornene (130 mg, 1.2 mmol) was dissolved in 2.5 mL of anhydrous dichloromethane in a 100 mL R.B.flask and to this two crystals of DMAP and 0.3 mL of anhydrous pyridine were added. To this solution 620 mg (2.7 mmol) of freshly prepared 3,5-dinitrobenzoyl chloride[160] was added and the flask capped with a $CaCl_2$ drying tube . The mixture was then strirred for 40 hours at room temperature. It was then quenched with 3 mL of water and the ester product was extracted with three 15 mL portions of dichloromethane. The dichloromethane layer was then washed with 10 mL saturated $CuSO_4$ solution, 10 mL of water and 10 mL of saturated brine solution. The solvent was then removed by rotary vacuum evaporation. The crude residue was subjected to dry silica column chromatography (1:40), using 20:80 ethyl acetate:petroleum ether. The first fraction to appear was the *endo* 3,5-dinitrobenzoate ester(**6.8**). Yield = 320 mg, 89%. Melting point 114.5 °C. The crystal for X-ray study was obtained by slow evaporation at room temperature of a solution in absolute alcohol.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.97 (s, 1H, H1) 6.46 (dd, 1H J = 2.9, 5.9 Hz, H2), 6.08 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.32 (s,1H, H4), 5.61 (dt,1H J = 1.5,2.9,6.3,7.8 Hz, H5x), 2.32 (m, 1H J = 3.9, 4.4, 8.3 Hz, H6x), 1.59 (m, 1H J = 1.5, 2.0, 5.4, 8.8 Hz, H6n), 1.44 (d, 1H J = 9.3 Hz, H7s), 1.14 (dt, 1H J = 2.9, 3.4, 6.3, 12.7 Hz, H7a), 9.20 (1H), 9.05 (2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 42.29(C1), 139.39(C2), 130.98(C3), 47.83(C4), 78.04(C5), 45.92(C6), 34.81(C7), 162.55(C8), 134.21(C9), 129.29(C10, C14), 148.58(C11, 13), 122.19(C12).

7.9 *endo*-Bicyclo[2.2.1]hept-5-en-2-yl 3-nitrobenzenesulfonate



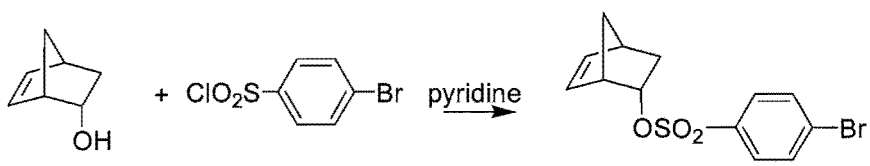
7.9

5-*endo*-Hydroxy-2-norbornene (300 mg, 1.2 mmol) was dissolved in 2.5 mL of anhydrous dichloromethane and 0.3 mL of anhydrous pyridine and two crystals of DMAP were added. To this solution 600 mg (2.7 mmol) of freshly prepared 3-nitrobenzenesulfonyl chloride was added. The flask was fitted with a $CaCl_2$ drying tube and the solution was stirred for 40 hours at room temperature. The reaction mixture was then quenched with 3 mL of water and the ester was extracted with four 15 mL aliquots of dichloromethane. The combined dichloromethane extracts were washed with 10 mL saturated $CuSO_4$ solution,10 mL water and finally with 10 mL saturated brine solution. The solvent was then removed by rotary evaporation and the crude product was purified by silica column chromatography (1:20), using 90:10 dichloromethane:petroleum ether. The first fraction collected consisted of the pure sulphonate ester(**6.9**). Yield = 0.265 mg (89%) m.p. 118°C. The crystal for X-ray study was obtained by slow evaporation of a solution in 1:1 dichloromethane/ethyl acetate.

^{1}H NMR (500 MHz, $CDCl_3$),δ 2.81 (d, 1H J = 1.0 Hz, H1), 6.32 (dd, 1H J = 2.9, 5.9 Hz, H2), 5.86 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.07(s, 1H, H4), 5.15 (m, 1H J = 2.4, 2.9, 3.9, 6.3, 8.3 Hz, H5x), 2.01 (m,1H J = 3.9, 4.4, 8.3, 12.7 Hz, H6x), 1.45 (m, 1H J = 1.5, 2.0, 3.9, 5.9, 7.8, 9.3 Hz, H6n), 1.22 (d, 1H J = 9.3 Hz, H7s), 1.03 (m, 1H J = 2.4, 3.9, 6.3, 12.7 Hz, H7a), 7.91 (1H),7.89 (1H),7.78 (1H),7.75 (1H), 7.69 (1H).

^{13}C NMR (75 MHz, $CDCl_3$) δppm 41.88(C1), 139.17(C2), 130.69(C3), 47.33(C4), 83.66(C5), 46.73(C6), 34.28(C7), 139.39(C8), 122.94(C9). 148.12(C10), 127.99(C11), 130.66(C12), 133.12(C13).

7.10 *endo*-bicyclo[2.2.1]hept-5-en-2-yl 4-bromobenzenesulfonate



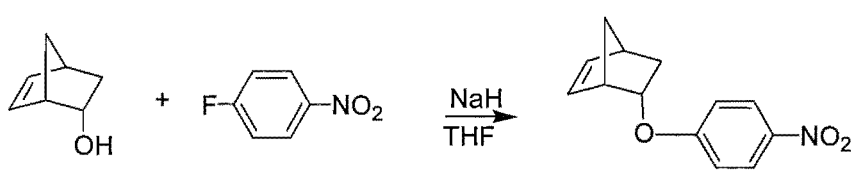
7.10

130 mg, (1.2 mmol) of 5-*endo*-hydroxy-2-norbornene were dissolved in 2.5 mL of anhydrous CH_2Cl_2 in a 100 mL R.B.flask and to this 0.3 mL of anhydrous pyridine and two crystals of DMAP were added. To the stirred mixture 600 mg (2.3 mmol) of freshly prepared 4-bromobenzenesulphonyl chloride[160] was added. The flask was fitted with a $CaCl_2$ drying tube and the solution was stirred for 40 hours at room temperature. It was then quenched by adding 3.5 mL of water and extracted four times with 15 mL of dichloromethane. The combined dichloromethane fractions were washed with 10 mL saturated copper sulphate solution, 10 mL water and 10 mL saturated sodium chloride solution. The solvent was then removed by rotary vacuum evaporation without drying. The residue was subjected to dry silica column chromatography (1:50) using 80:20 petroleum ether:ether as eluent. The first fraction to emerge consisted of impurities. The next fraction was the *p*-bromobenzenesulphonate ester. This also showed traces of impurities (NMR). To remove these it was recolumned using 90:10 dichloromethane:petroleum ether as eluent. This gave the pure ester product (**6.10**). The yield was 305 mg (78%) m.p. 87 °C. This was then crystallized from ethyl acetate.

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.82 (s, 1H, H1), 6.33 (dd, 1H J = 3.2, 5.9 Hz, H2), 5.87 (dd, 1H J = 2.8, 5.5 Hz, H3), 3.07 (s,1H, H4), 5.16 (m,1H J = 2.4, 2.8, 3.6, 6.3, 7.9 Hz, H5x), 2.02 (m, 1H J = 3.6, 4.4, 7.9, 12.7 Hz, H6x), 1.04 (m, 1H J = 2.4, 2.8, 4.0, 6.3, 12.7 Hz, H6n), 1.46 (m, 1H J = 2.0, 4.0, 5.9, 7.9 Hz, H7s), 1.22 (d, 1H J = 9.1 Hz, H7a), 7.76 (m, 2H), 7.69 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 41.89(C1), 138.94(C2), 130.91(C3), 47.29(C4), 82.76(C5), 46.65(C6), 34.27(C7), 136.34(C8), 132.47(C9, C13), 129.23(C10, C12), 128.71(C11).

7.11 *endo*-Bicyclo[2.2.1]hept-5-en-2-yl 4-nitrophenyl ether



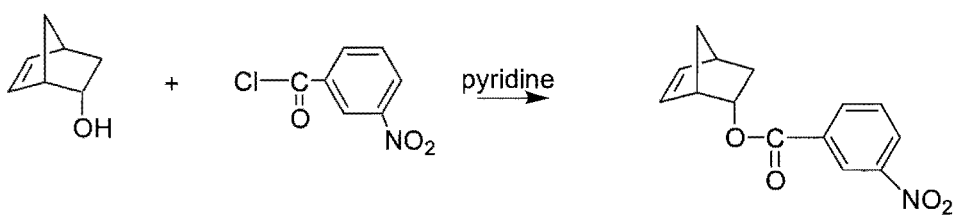
7.11

5-*endo*-Hydroxy-2-norbornene (110 mg, 1 mmol) was dissolved in 10 mL of anhydrous DMSO (dried over 4A molecular sieves for 24 hours). To this solution, 200 mg, (8.3 mmol) of sodium hydride was added and the mixture was heated on a water bath at 80 °C for 4hours. The mixture was then cooled to room temperature and 550 mg, (3.9 mmol) of 4- fluoronitrobenzene was added. The solution was stirred at room temperature for 18 hours[81,183]. It was then quenched with 10 mL of water and the ether formed was then extracted three times with 15 mL portions of dichloromethane. The combined extracts were dried over anhydrous Na_2SO_4 and vacuum rotary evaporated. The crude product was then subjected silica column using the 80:20 petroleum ether:ether as eluent. The first fraction off the column was the *endo* ether (**6.11**) contaminated with a small amount (15%) of the *exo* isomer. Yield = 230 mg, 78%. Attempts to obtain crystals of pure *endo* isomer for X-ray study gave only ones of the *exo* form. It is possible that the *endo* derivative was too low melting to give crystals.

^{1}H NMR (500 MHz, $CDCl_3$), δ 2.94 (s, 1H, H1), 6.37 (dd, 1H J = 2.9,5.9 Hz, H2), 6.05 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.28 (s, 1H, H4), 4.99 (m, 1H J = 2.9, 3.4, 4.4 Hz, H5x), 2.23 (m, 1H J = 3.4, 3.9, 4.4, 12.2 Hz, H6x), 1.56 (m, 1H J = 2.0, 4.4, 5.9, 7.8 Hz, H6n), 1.41 (t, 1H J = 5.9, 8.8 Hz, H7s), 1.07 (dt, 1H J = 2.9, 3.4, 5.9 Hz, H7a), 8.17 (2H), 6.91 (2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 42.43(C1), 138.54(C2), 131.59(C3), 46.09(C4), 79.16(C5), 47.41(C6), 35.09(C7), 163.71(C8), 125.82(C9, C13), 115.20(C10, C12), 141.15(C11).

7.12 *endo* Bicyclo[2.2.1]hept-5-en-2-yl 3-nitrobenzoate



7.12

5-*endo*-hydroxy-2-norbornene (90 mg, 0.82 mmol) was dissolved in 2.5 mL of anhydrous dichloromethane in a 100 mL R.B. flask and two crystals of

DMAP and 0.3 mL of anhydrous pydrine were added. To this mixture 650 mg (2.5 mmol) of freshly prepared 3-nitrobenzoyl chloride was added. The flask was stoppered and the contents stirred for 24 hours at room temperature. The reaction mixture was quenched with 3 mL of water and the crude ester product was extracted with dichloromethane (15 mL, three times). The dichloromethane fractions were then washed with 10 mL of saturated copper sulphate solution, 10 mL of water and finally with 10 mL of saturated brine solution. The dichloromethane was then dried over anhydrous $MgSO_4$, and solvent removed by vacuum rotary evaporation. The crude residue was purified by dry silica column chromatography (1:30) using 80:20 petroleum ether:ethyl acetate as eluent. The fraction coming off first was pure 3-nitrobenzoate ester of 2-*endo*- norbornenol (**6.12**). The yield was 190 mg (89%). The product was semi-solid at room temperature. Crystals were obtained by the slow evaporation of a solution in DCM at room temperature.

^{13}HNMR (500 MHz, $CDCl_3$), δ 2.94 (s,1H,H1), 6.42 (dd, 1H J = 2.9, 5.4 Hz, H2), 6.08 (dd, 1H J = 2.9, 5.4 Hz, H3), 3.30 (s, 1H, H4), 5.57 (dt, 1H J = 2.9, 3.4, 7.8, 11.7 Hz, H5x), 2.29 (m, 1H J = 3.4, 3.9, 4.9, 8.3 Hz, H6x), 1.56 (m, 1H J = 2.0, 2.9, 3.9, 6.8, 8.8, Hz, H6n), 1.43 (d, 1H J = 9.3 Hz, H7s), 1.12 (dt, 1H J = 2.9, 3.4, 6.3 Hz,H7a), 8.76 (t, 1H J = 2.0, 3.9 Hz), 8.40 (dt, 1H J = 0.98, 1.5, 2.0, 3.4 Hz), 8.29 (d, 1H J = 7.8 Hz), 7.63 (t, 1H J = 7.8, 8.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$), δ 42.28(C1), 138.97(C2), 131.24(C3), 47.73(C4), 76.77(C5), 45.92(C6), 34.79(C7), 164.52(C8), 124.42(C9), 135.15(C10), 127.18(C11), 129.49(C12), 132.27(C13)

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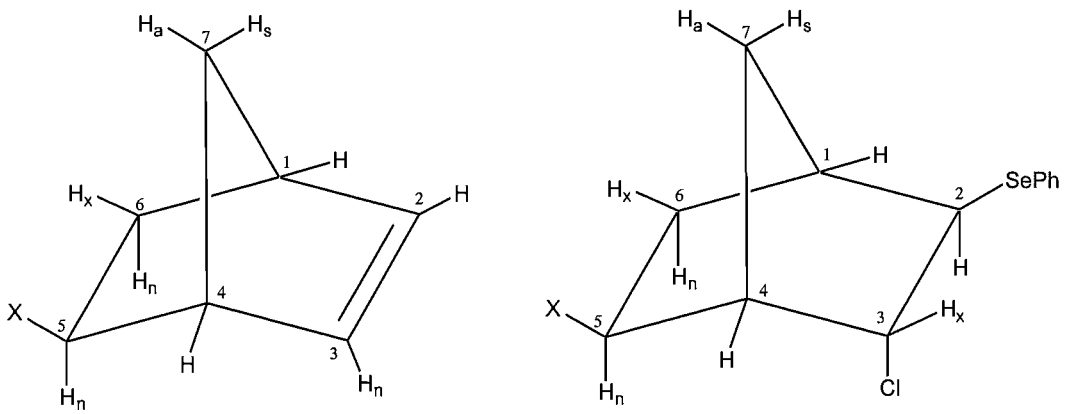
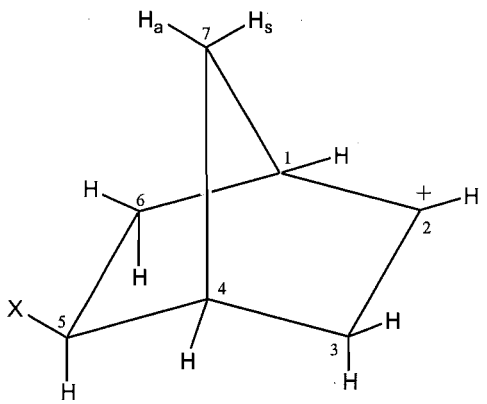
Appendix. The Numbering of the skeleton in [2.2.1]bicycloheptanes and [2.2.1]bicycloheptenes and their derivatives.

Part 2 of this thesis is concerned with addition reactions of substituted 2-norbornenes to give saturated [2.2.1]bicycloheptanes derivatives as products. Unfortunately the numbering systems used for for the six membered ring in the two classes of compound, although the same in the parent compound, can change once substituents are introduced. In both cases the numbering starts from one of the bridging carbons and proceeds round the 6-membered ring. The decision as to which of the two bridging carbons is C1 in bicyclo[2.2.1]heptanes is made in the same way as in straight chain compounds and is based on minimising the numbers assigned to the carbons bearing the substituents. Our parent norbornene on this basis must be 2-norbornene, and a compound bearing a substituent X on one of the CH_2 groups of the 6-membered ring will be a 5-X-substituted 2-norbornene, rather than a 6-substituted one because 5 is less than 6. Once addition to the double bond has taken place the the possibility of complications arises, because the group X may change the numbering. To circumvent this problem in Part 2 it was decided to name all substituents using prefixes, which leads to the consisten numbering system below, for example.

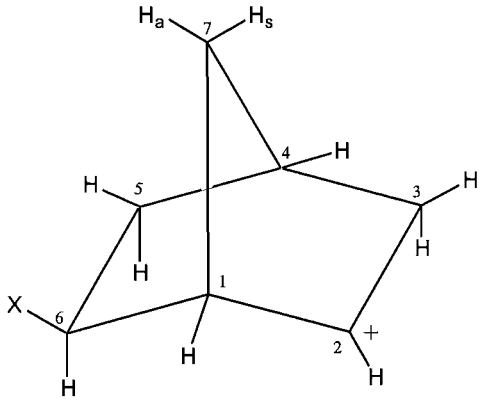


In listing ^1H chemical shifts for norbornane derivatives it is customary to indicate whether these occupy *exo* or *endo* positions by using 'x' and 'n' respectively as indicators. In the same way the hydrogens at C7 are assigned as 'a' or 's' depending on whether they are directed towards or away from the fuctional

groups in the ring. A possibility for confusion arose whenever the subject of 2-norbornyl carbocations comes up. In the 2-norbornyl cation the numbering still must start from one of the bridging carbons, but C2 must be the cationic one. If the cationic generated at C2 in the above system, there is no problem — the carbon bearing the substituent X is still C5. However if it is the one at C3, then the numbering system must change to accommodate this.



Original numbering



preferred numbering

This means that when one is considering potential bonding interactions between C3 and C5 of an X-substituted norbornene in Part 1, one is comparing them with the same interactions between C2 and C6 in a 2-norbornyl cation. This is a particular problem when one is considering resonance forms in Part 1. In Part 2, when one considers the structure of the seleniranium cationic intermediate, whether X is bonded to C5 or C6 could be regarded as uncertain.

The numbering used in assigning ^{1}H and ^{13}C NMR spectra is that given on the previous page. In general all carbons in the ^{13}C spectrum were assigned, but in the ^{1}H spectrum this was only done for the protons of the alicyclic system. In those compounds where an aromatic nucleus was present the the ring was numbered as shown below.